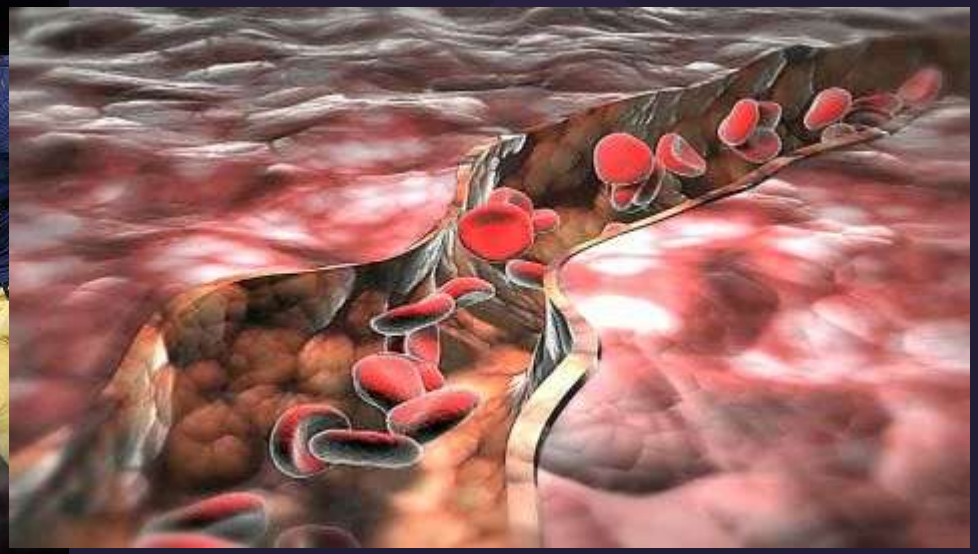
MBD
Does HDF Help

HESHAM ELSAYED

PROF OF NEPHROLOGY AIN SHAMS UNIVERSITY

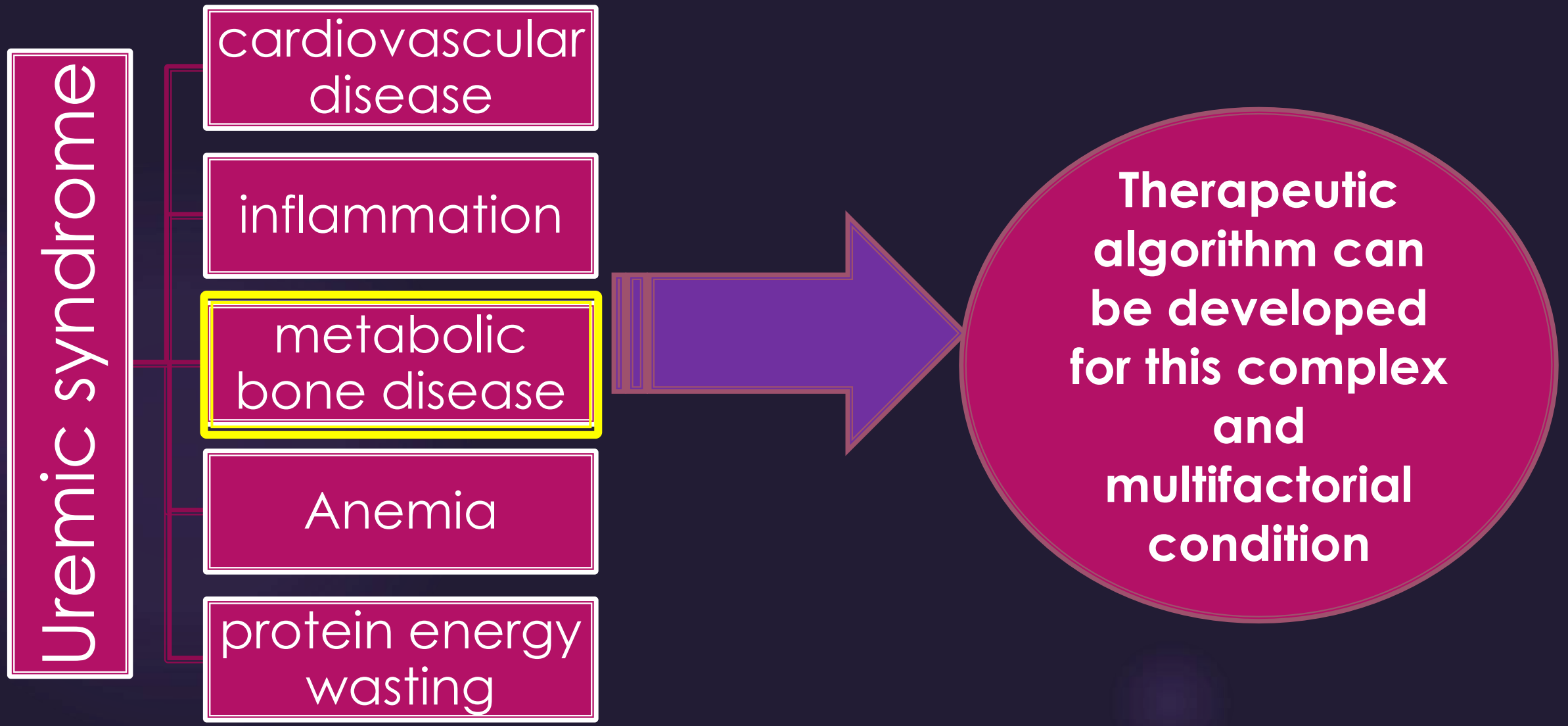
CKD-MBD MANY PLAYERS WITH THE SAME TARGET

Targeting



Inflamed ET

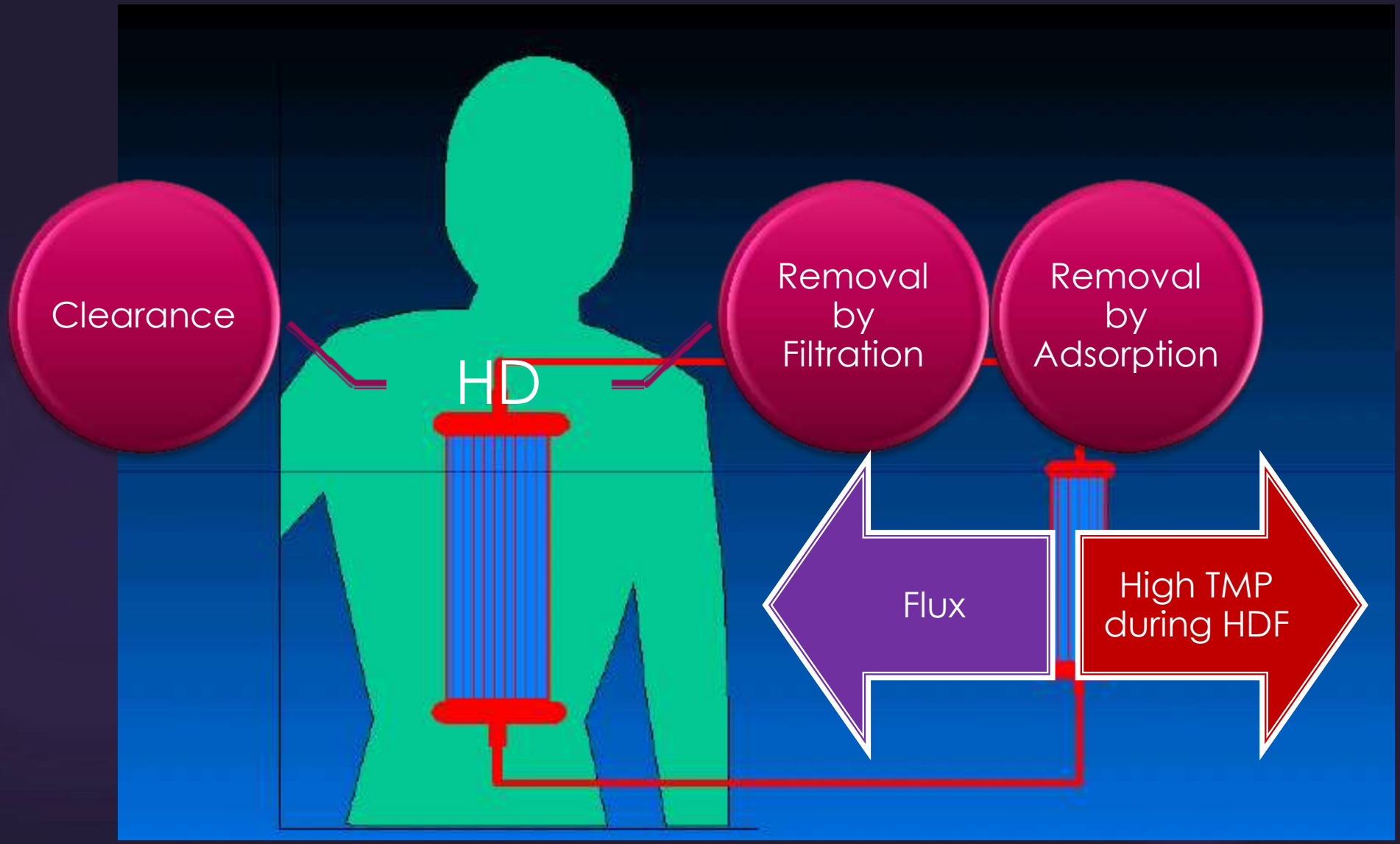
The uremic syndrome (the lancet Mar 2, 2016)



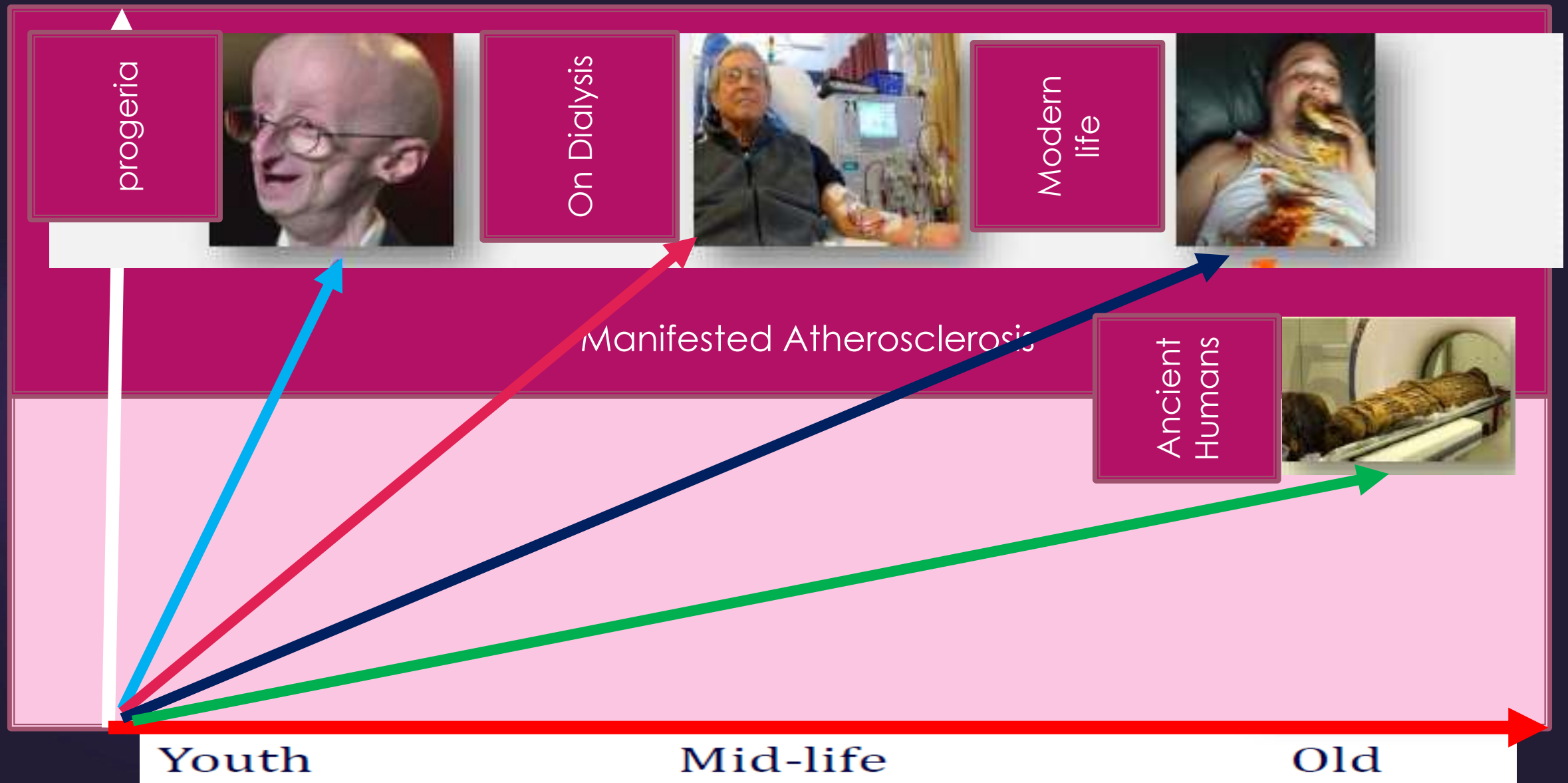
Therapeutic challenges in Reversing the Attack of the Endothelial cells

Therapeutic challenges in Reversing the Attack of the Endothelial cells

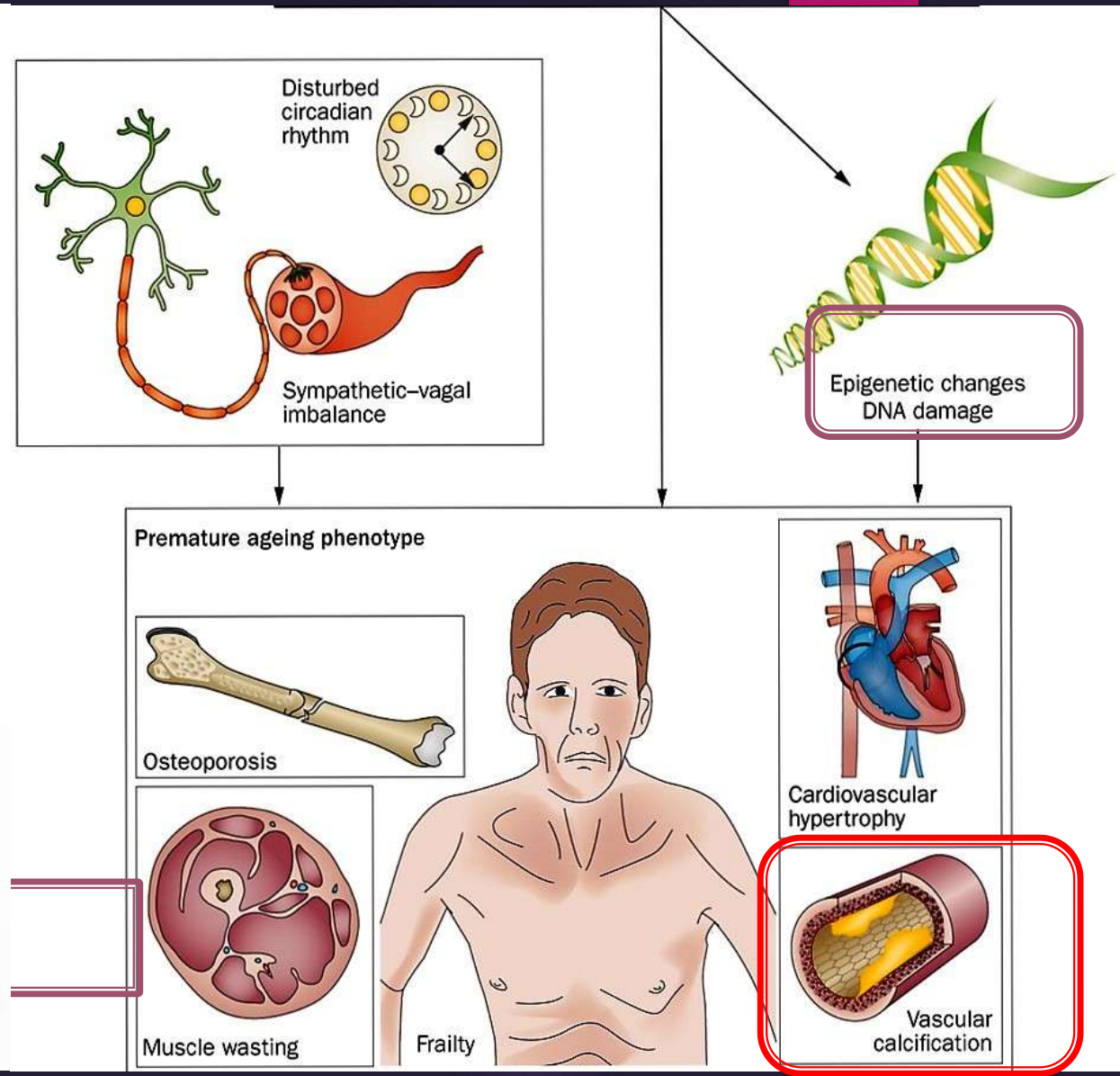
HD : a Filtration Therapy



Models of Vascular Aging



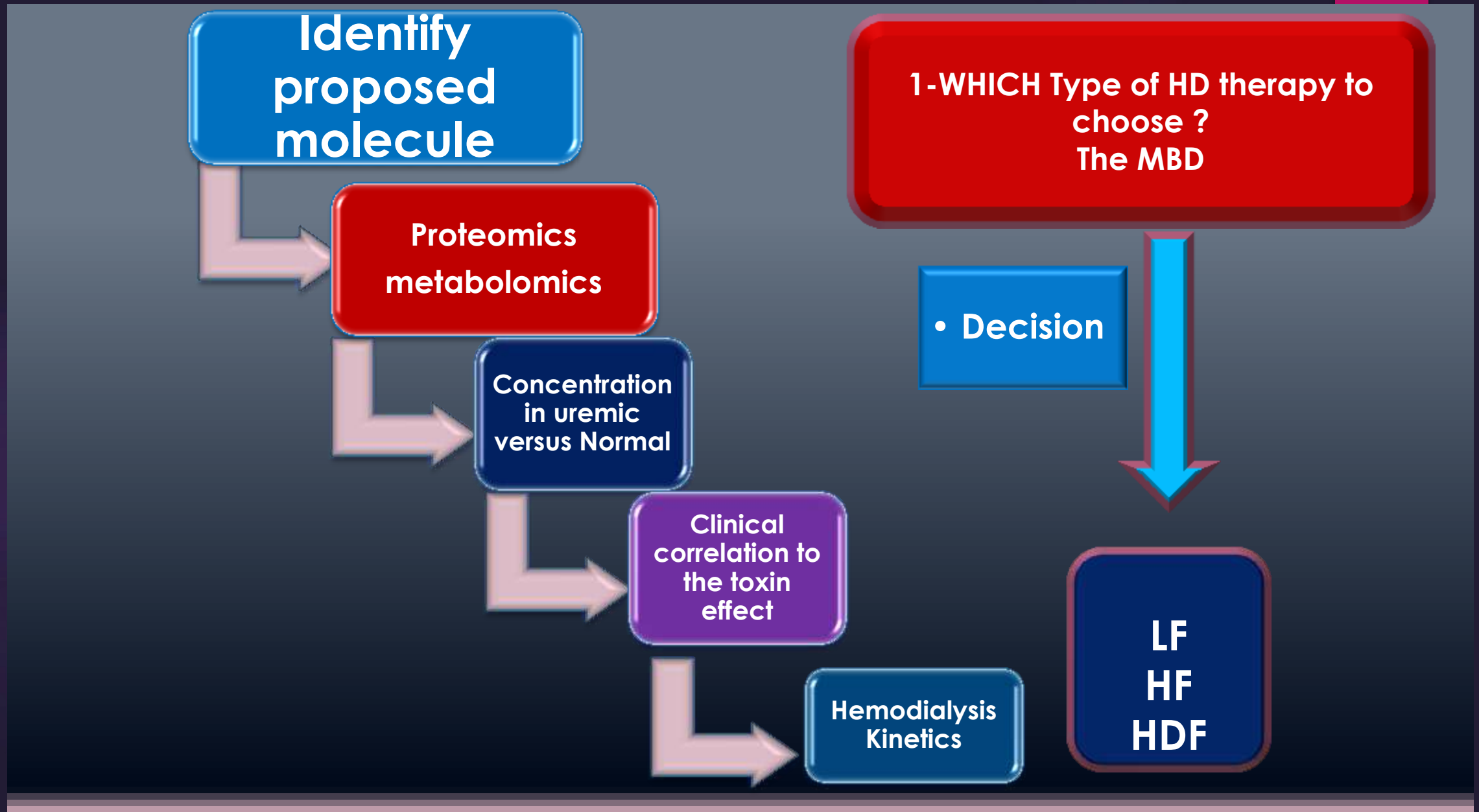
Chronic Kidney Disease:



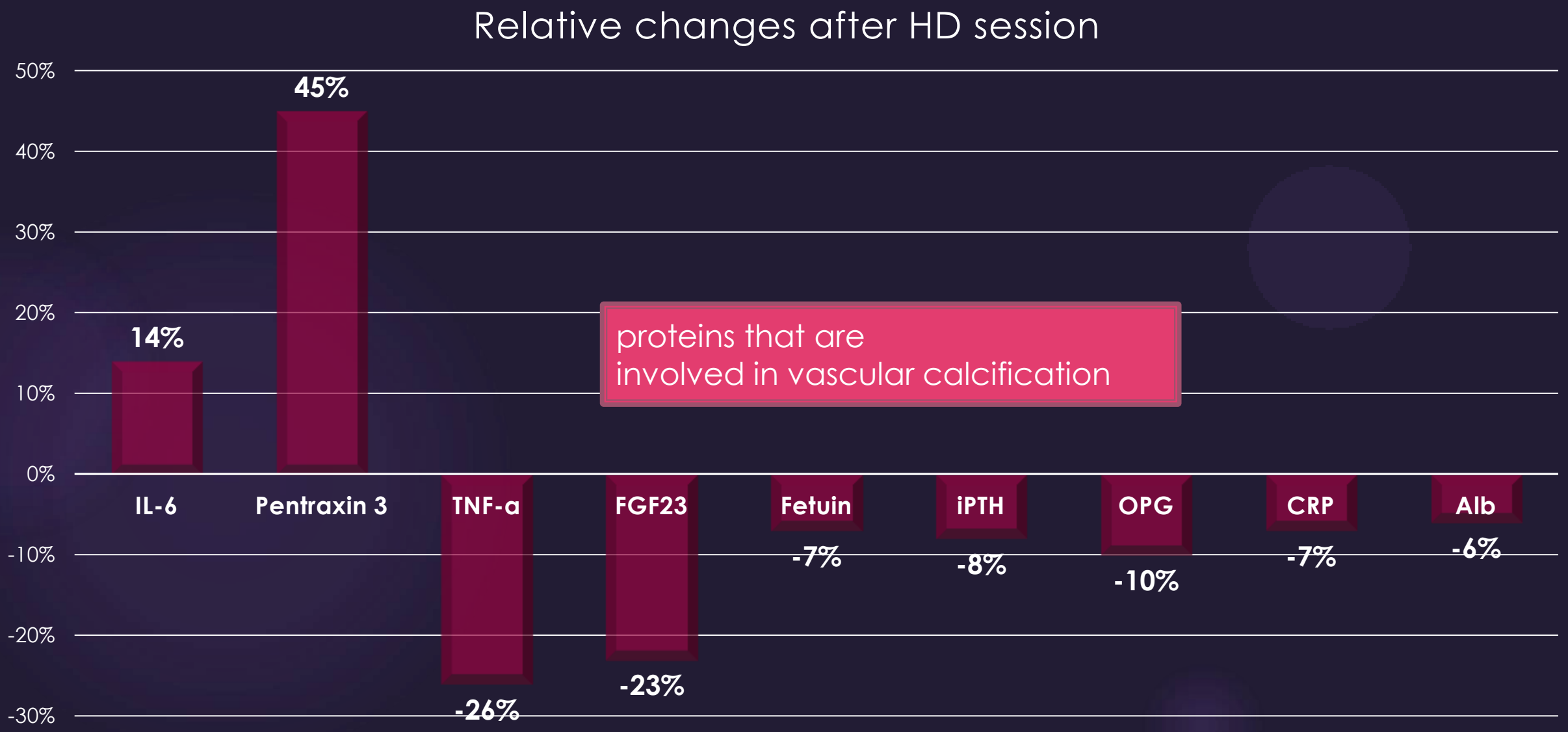
MW of the common players

Markers	MW
B2m	11800 D
iPTH	9500 D
Scelrostin	23,000 D
FGF 23	32,000 D
Osteoprotegerine	60,000 D in monomer 120,000 D in dimer
CRP	115,000 D
Soluble Klotho	130,000 D

Approach for HD therapy : MBD



Changes in circulating biomarkers during a single hemodialysis session Hemodialysis International 2012;



Porosity or Pressure ?

Contrib Nephrol. 2015;185

more easily achieved

SUPERFLUX Type V

- RR of β2-MG >80%
- RR α1-MG being >35%

OL-HDF

- RR of β2-MG >80%
- RR α1-MG being >35%

Hemodialysis International 2005; 9: 409–415

Hyperphosphatemia among end-stage renal disease patients in developing countries: A forgotten issue?

Adel AFIFI,[1] Hesham EL-SAYED,[1] Maged EL-SETOUHI,[2] Hayam AHMED,[1] Noha KHALIFA[1]

[1]Department of Internal Medicine and Nephrology, Ain Shams University, Cairo, Egypt; [2]Department of Community Medicine and Public Health, Ain Shams University, Cairo, Egypt

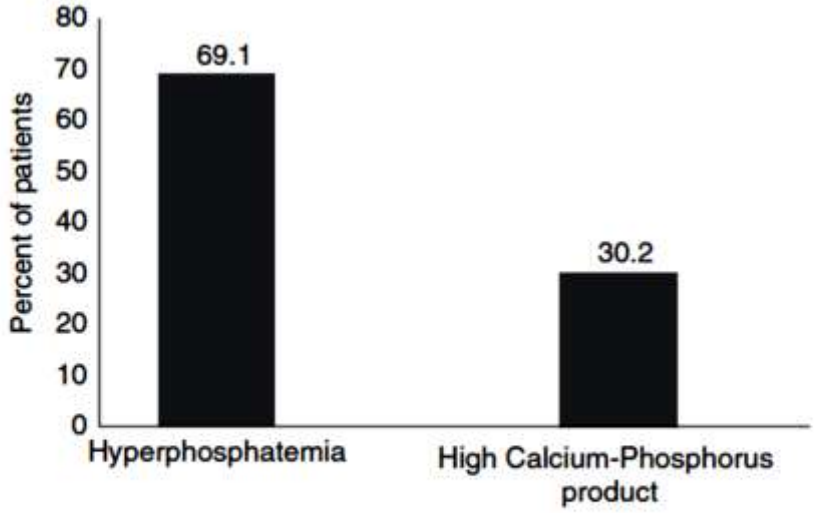
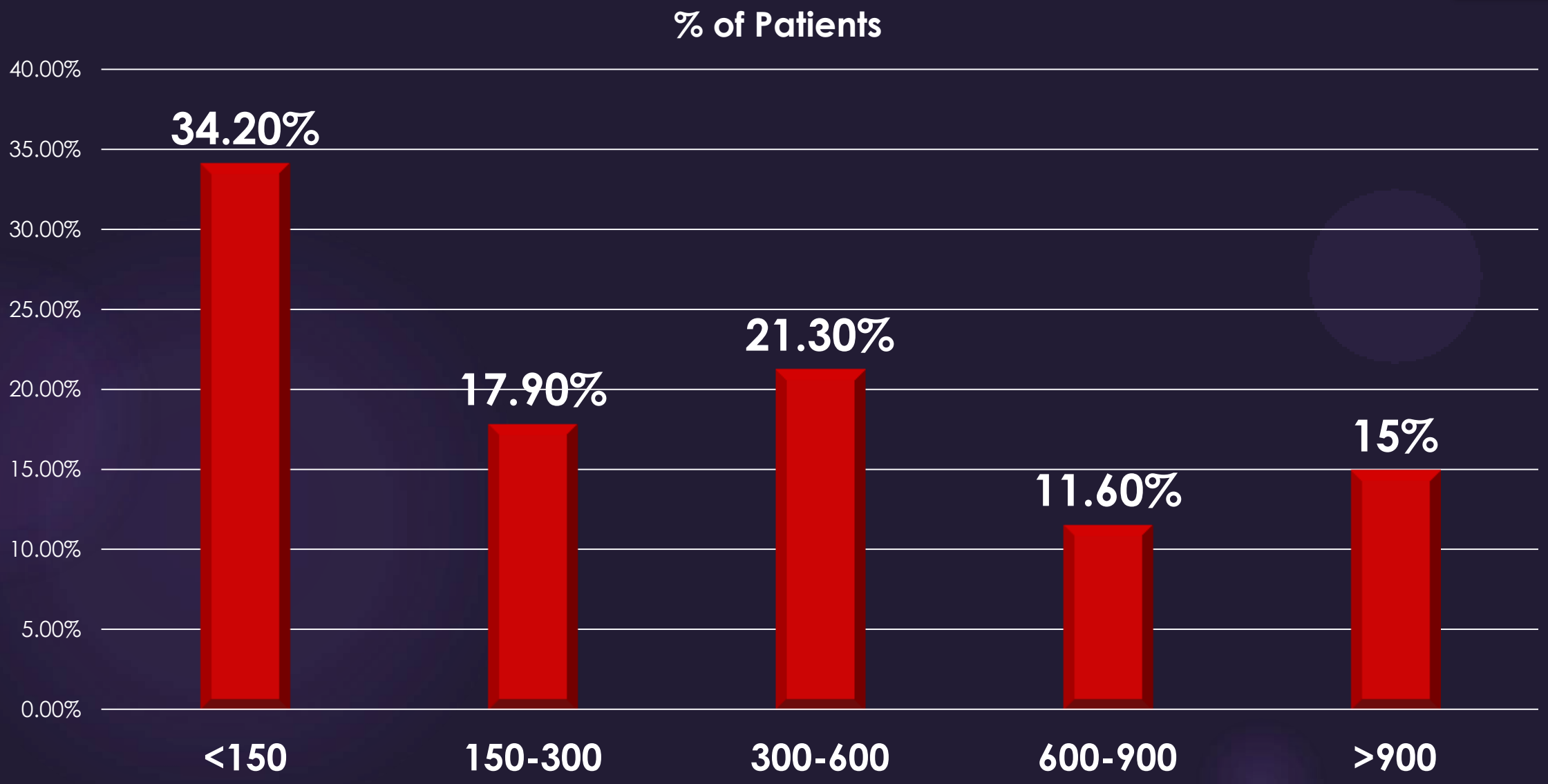


Figure 1 Percentage of high serum phosphorus and high calcium–phosphorus product.

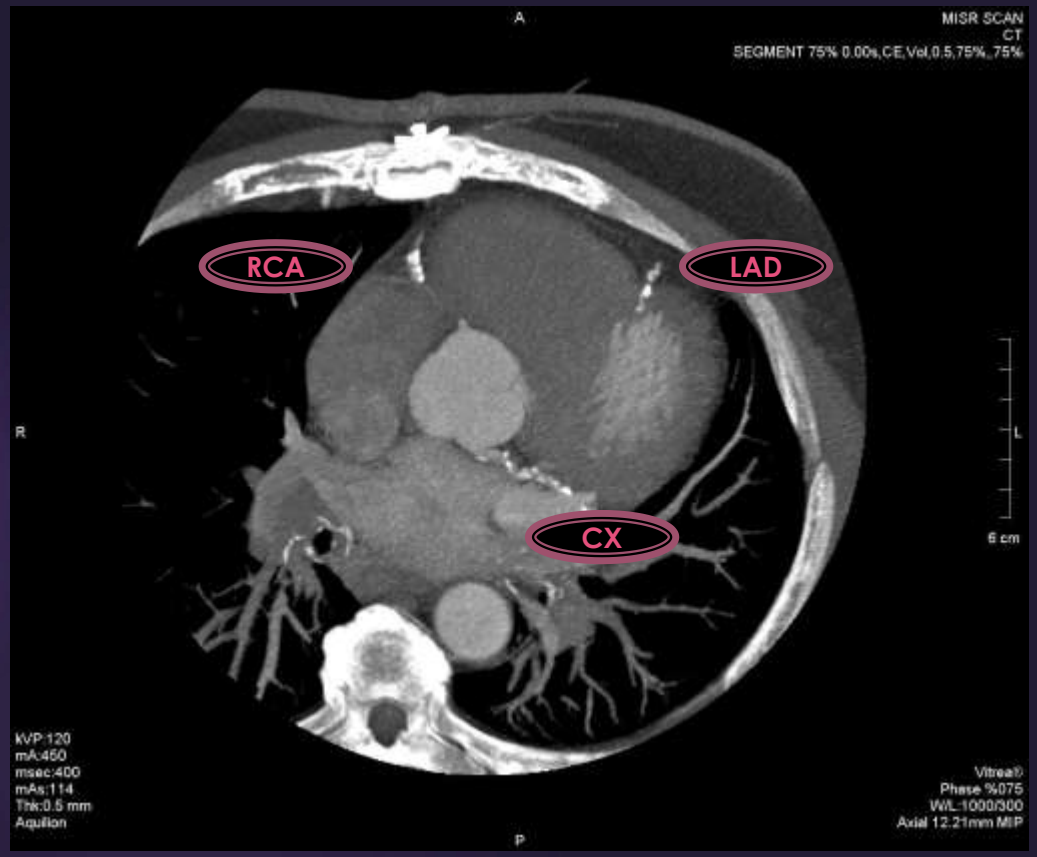
Serum iPTH among 2839 HD Egyptian patients

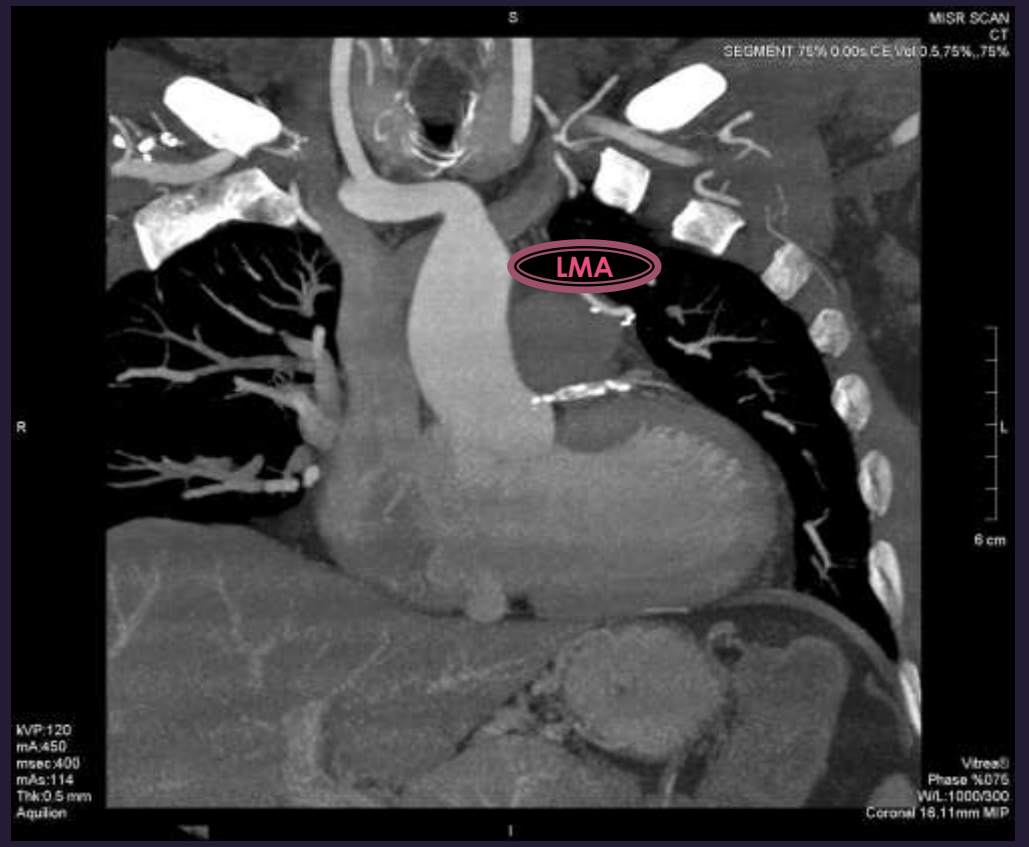


Coronary artery calcification among 60 patients at ASUH (Afifi A.,Elsayed H.,Elsaid T. 2006)

	No or minimal Calcification (CAS ≤10) N=43	Mild Calcification (CAS 10-100) N=7	Moderate to severe Calcification (CAS >100) N=10	P
Calcium	7.99±0.80	8.08±0.31	8.30±0.37	NS
Phosphorus	5.82±1.22	6.15±1.20	6.77±0.97	NS
Ca x P	46.37±10.66	49.67±9.27	56.00±7.36	0.029
CRP	13±17.97	23.57±18.50	32.60±35.92	0.023
Homocysteine	20.93±6.45	19.42±4.97	21.55±2.59	NS

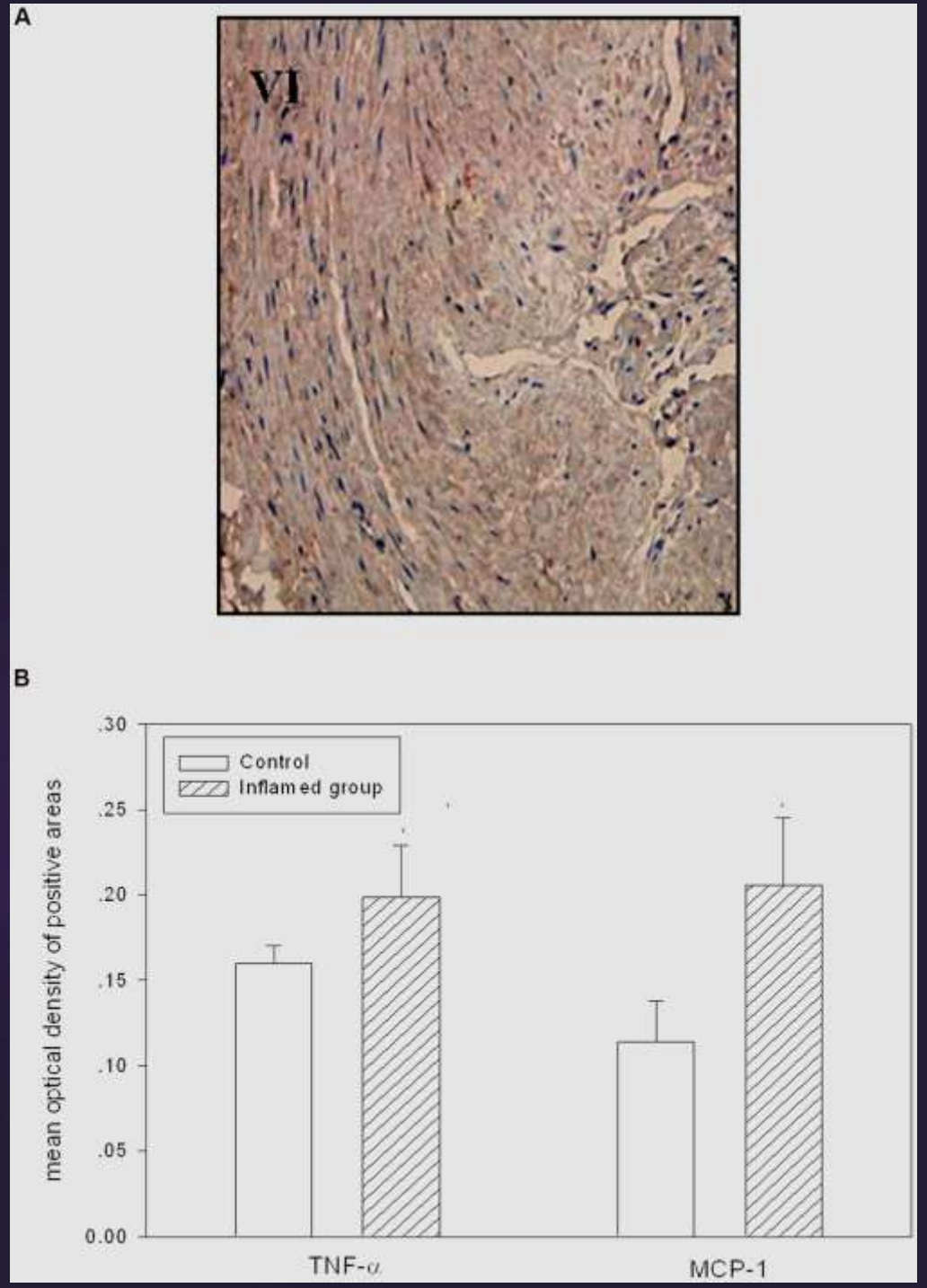
40% OF the patients Had Coronary calcification





Calcification follows inflammation in human atherosclerosis and therefore most likely represents a secondary phenomenon.

Nephrol. Dial. Transplant. (2015) 30 (3): 352-357.

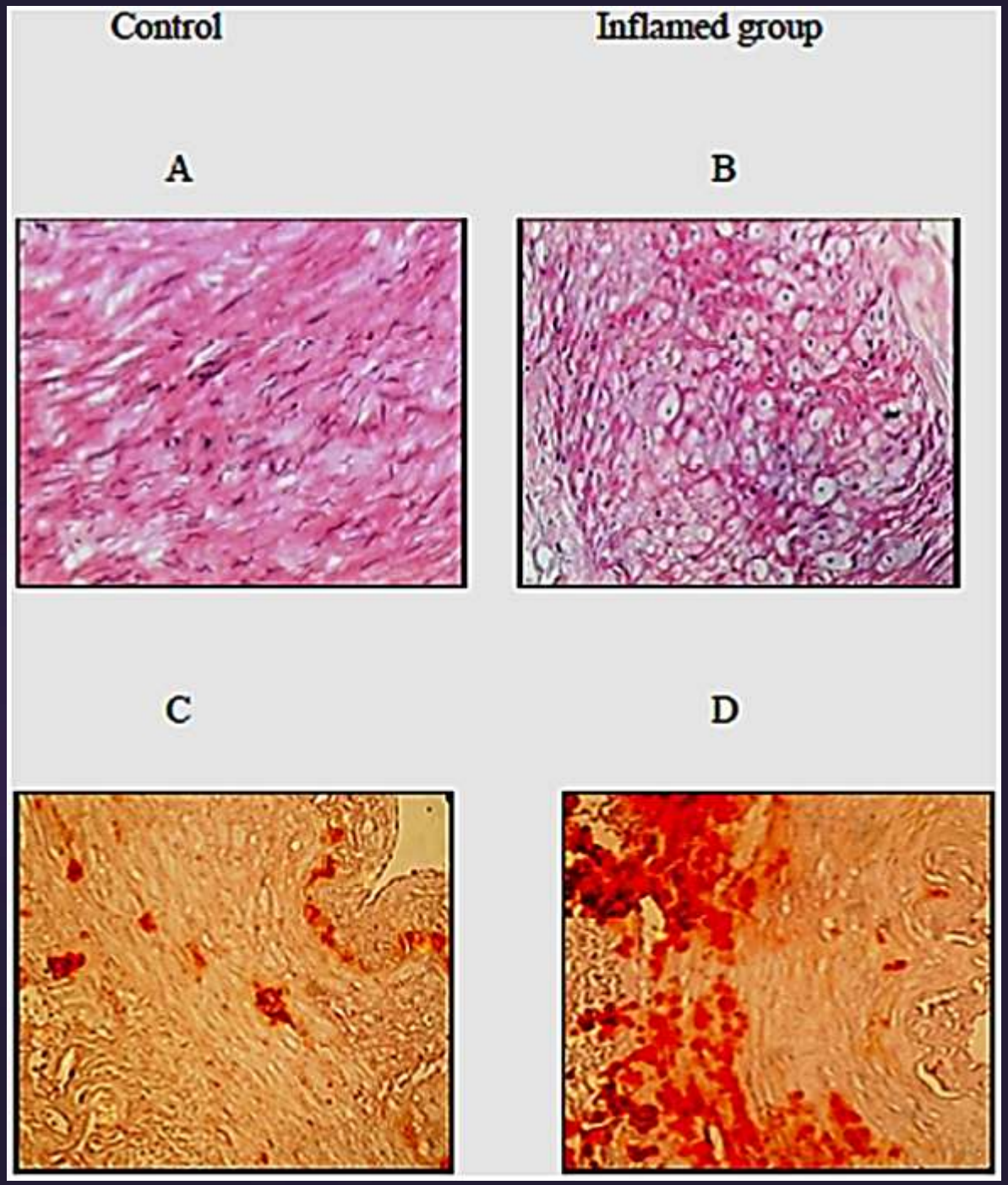


International Journal of CARDIOLOGY

The expression of tumour necrosis factor-a (TNF-a) and monocyte chemotactic protein-1 (MCP-1) of the radial artery are increased in the inflamed Patients immunohistochemical staining

+ve correlation with CRP

October 2011Volume 152



International Journal of CARDIOLOGY

Inflammation Disrupts the LDL Receptor Pathway and Accelerates the Progression of Vascular Calcification in ESRD Patients

Calcification was examined by alizarin red S staining, and calcium deposits were stained orange-red

October 2011Volume 152

Review

Blood Purification

Blood Purif 2015;40(suppl 1):12–16
DOI: 10.1159/000437405

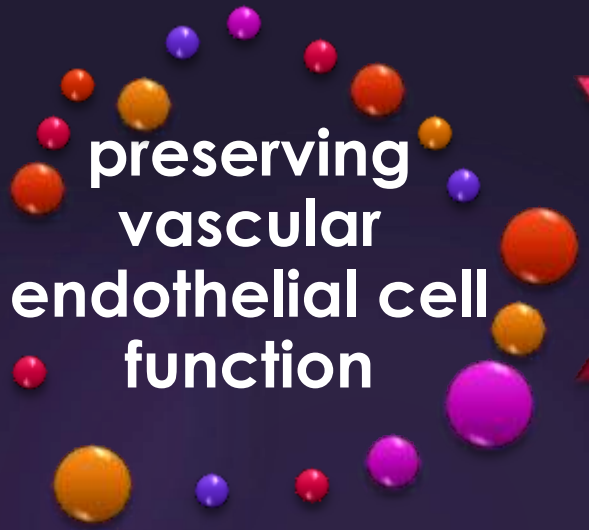
Published online: September 8, 2015

Clinical Expectation of Online Hemodiafiltration: A Japanese Perspective

Tadao Akizawa[a] Fumihiko Koiwa[b]

[a]Division of Nephrology, Department of Medicine, Showa University School of Medicine, Tokyo, and [b]Division of Nephrology, Department of Medicine, Showa University Fujigaoka Hospital, Yokohama, Japan

HDF Japanese Perspective Blood Purif 2015;40



Nephrol Dial Transplant 2014; 29:

reduction in fibroblast growthfactor-23

improvement of the nutritional status by reducing inflammatory stress

Amplifiers in CKD-MBD

Possible HDF key

Sterile dialysate

Molecule removal

inflammation

UREMIC TOXINS

ET

MALNUTRITION

Endothelial dysfunction

ROS

CKD – MBD

KEY POINT:

The presence and magnitude of arterial and valvular calcification are strongly associated with cardiovascular morbidity and mortality. Risk reduction may be achieved with a tailored, multifactorial approach to MBD: [3,4]

- Calcium or non-calcium-based phosphate binders
- Patient education
- CVD risk reduction measures
- Active vitamin D therapies
- Calcimimetic therapy
- Increased hemodialysis frequency, session time, dialyzer surface area and/or treatment type (eg, hemodiafiltration)

CKD - MBD

KEY POINT:

Traditional cardiac risk factors do not appear to entirely account for the elevated CVD morbidity seen in advanced CKD. Hyperphosphatemia, elevated Ca x P product, and hyperparathyroidism have been associated with CVD risk and mortality in advanced CKD. In addition, uremia is believed to confer non-traditional CVD risks (eg, a proinflammatory state and dysregulation of calcification inhibitors and inducers).[10,11]

Annual Dialysis Conference.. Seattle 2016

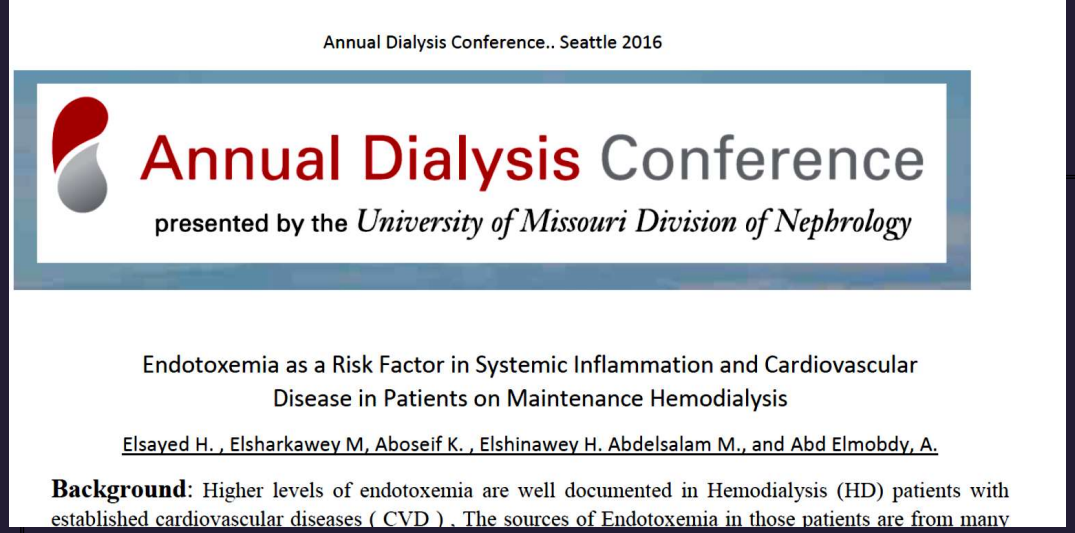
Annual Dialysis Conference

presented by the *University of Missouri Division of Nephrology*

Endotoxemia as a Risk Factor in Systemic Inflammation and Cardiovascular Disease in Patients on Maintenance Hemodialysis

Elsayed H. , Elsharkawey M, Aboseif K. , Elshinawey H. Abdelsalam M., and Abd Elmobdy, A.

Background: Higher levels of endotoxemia are well documented in Hemodialysis (HD) patients with established cardiovascular diseases (CVD) , The sources of Endotoxemia in those patients are from many



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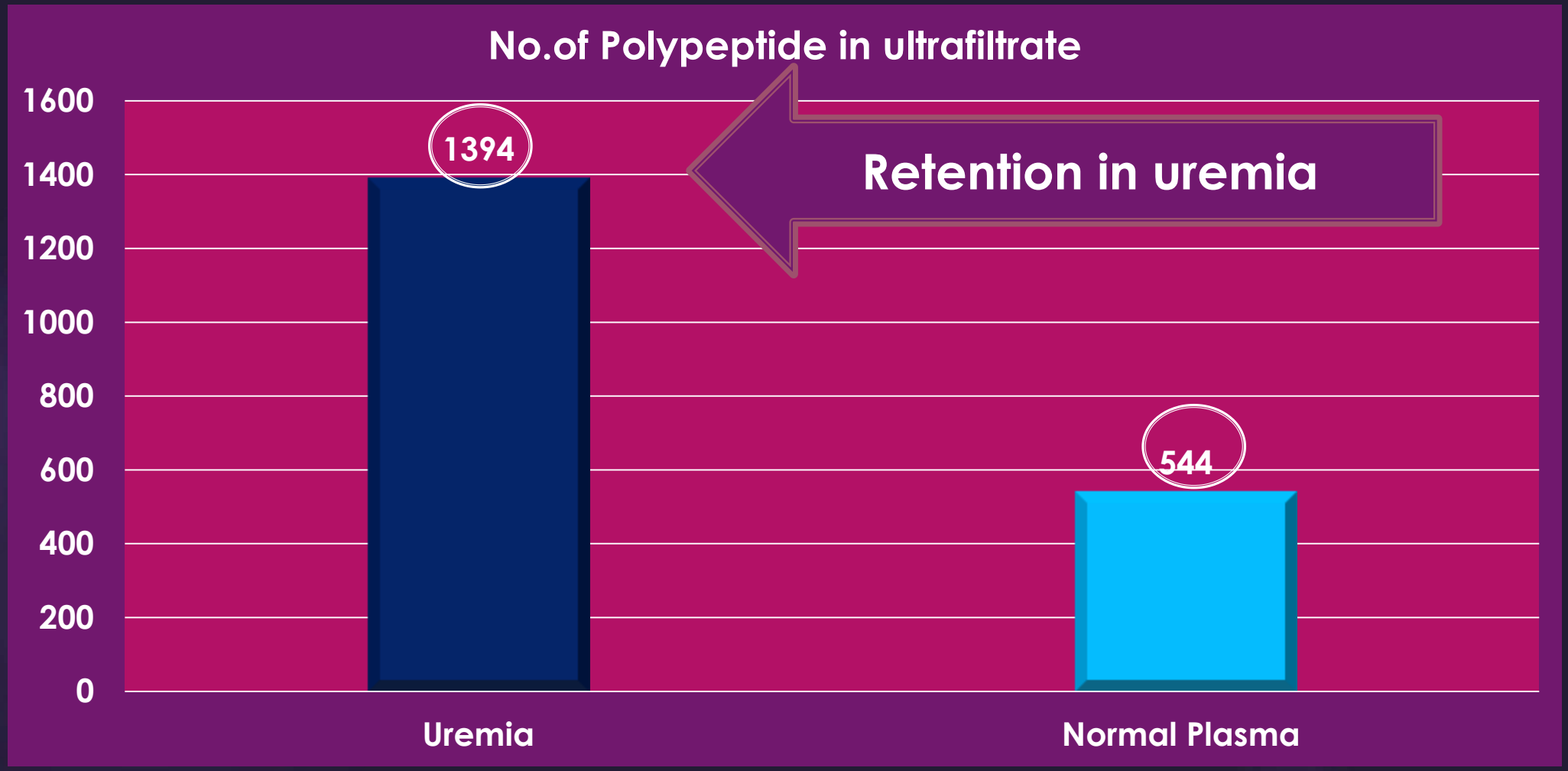
		Control group No CVD (Group B)	Patients group + CVD (Group A)	Independent t-test	
				T	P-value
Endotoxin predialysis (Eu/ml)	Mean ± SD	0.29 ± 0.12	0.36 ± 0.07	3.903	0.001
	Range	0.09 – 0.5	0.1 – 0.45		
Endotoxin postdialysis (Eu/ml)	Mean ± SD	0.31 ± 0.11	0.27 ± 0.12	1.903	0.059
	Range	0.1 – 0.52	0.1 – 0.63		
Endotoxin delta change	The same	21 (35.0%)	27 (45.0%)	2.552	0.279*
	Decrease	16 (26.7%)	18 (30.0%)		
	Increase	23 (38.3%)	15 (25.0%)		

Elsayed etal , ADC February 2016

Identifying the players

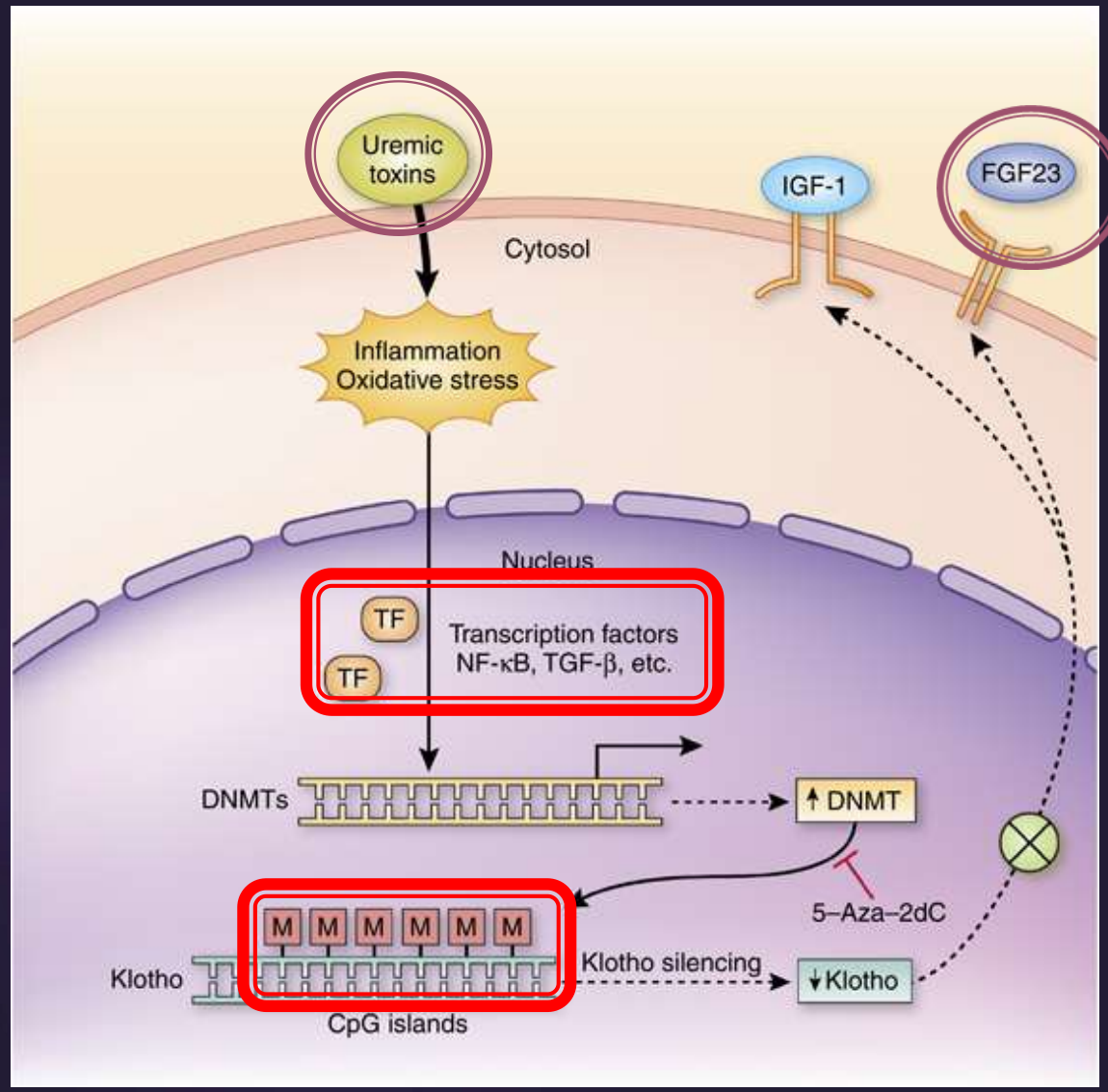
Weissinger E M et al. Nephrol. Dial. Transplant. 2004;19:3068-3077

Differences in Polypeptide between Uremic and Normal plasma using HF membrane Ultrafiltrate



ROLE OF UREMIC TOXINS : Effect on KLOTHO Gene

JASN December 4, 2014



Uremic Toxins

induce DNA methyltransferase (DNMT) protein expression,

Hypermethylated status of *KLOTHO*

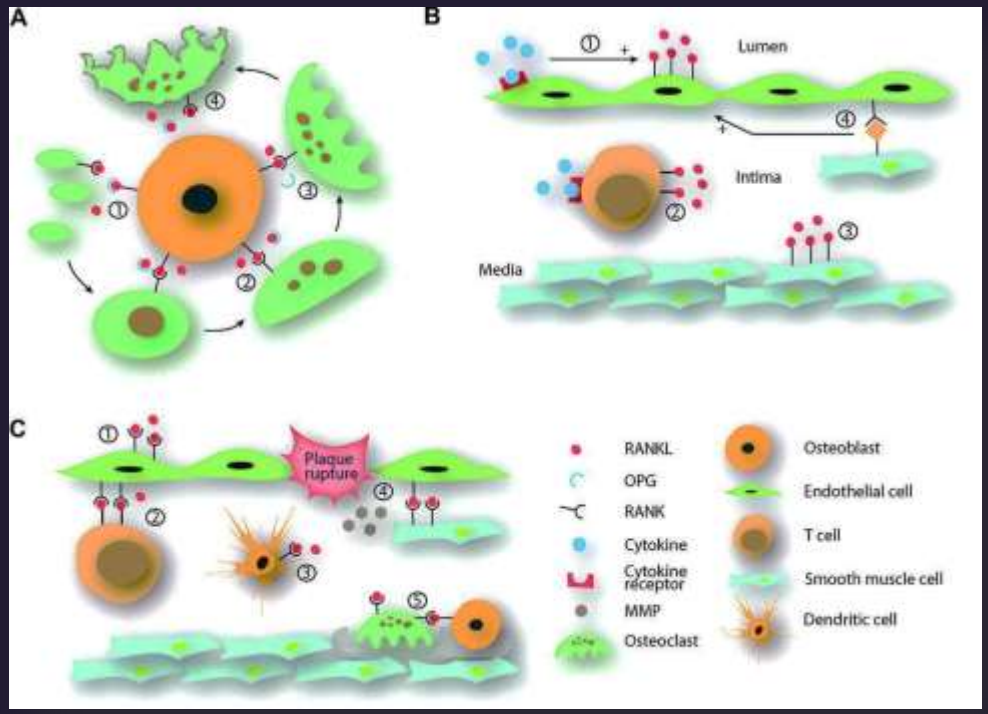
Biomarkers of vascular calcification and mortality in patients with ESRD Clin J Am Soc Nephrol. 2014 Apr;9(4):

High osteoprotegerin (OPG) tumor necrosis factor (TNF) receptor superfamily.

Potent osteoclastogenesis inhibitory activity

Low S.Fetuin

promotion of osteogenesis, leading to synthesis of bone proteins and matrix calcification within the arterial vesseL



vascular SMCs undergoing osteogenic differentiation

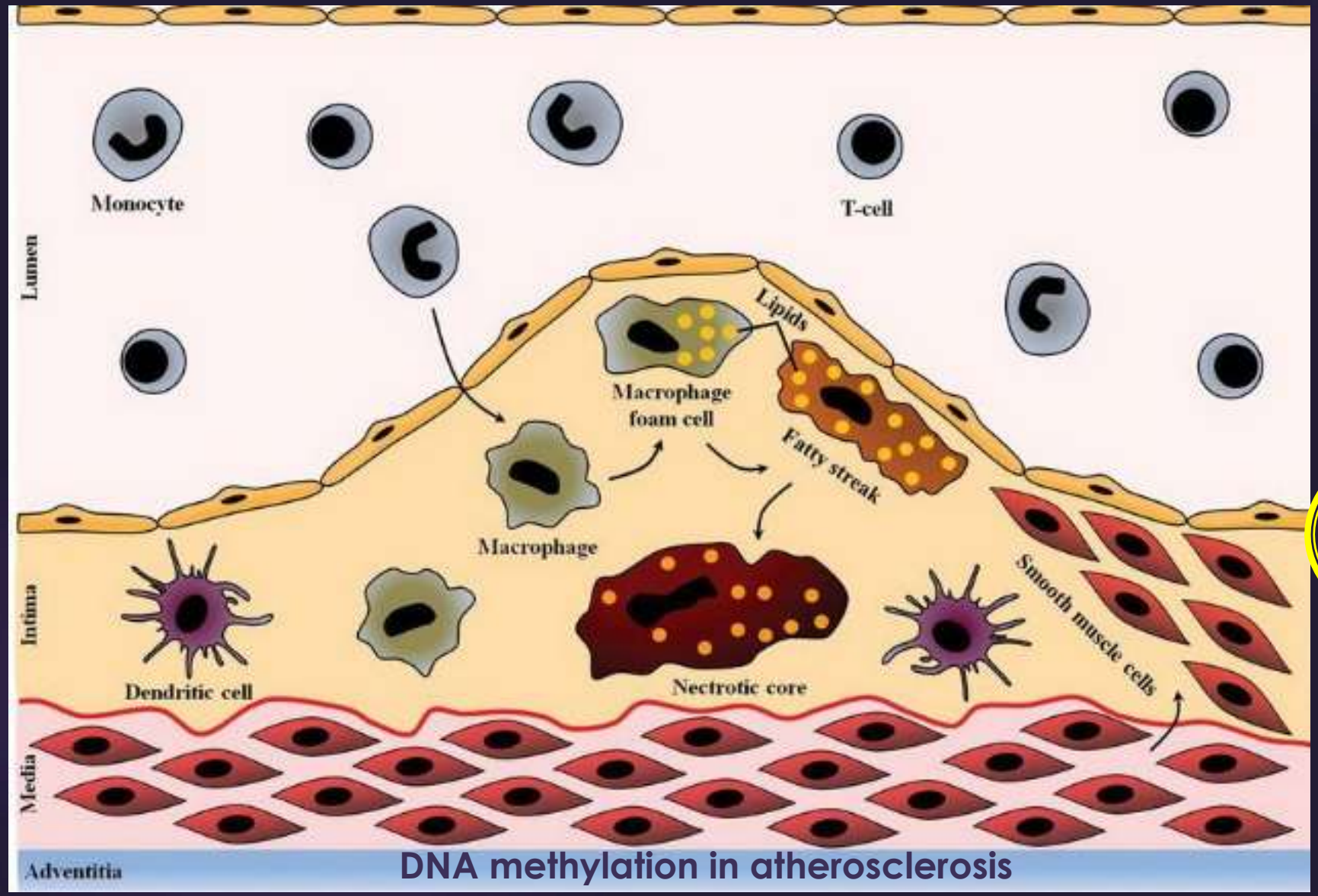
KLOTHO – FGF23 ORCHESTRA

FGF23 and klotho

- **Kidney**
  - inhibition of proximal tubular phosphate reabsorption
  - inhibition of 25(OH)-vitamin D 1a-hydroxylase
    - Loss Suppress Phosphate absorption in GIT in uremia
- **parathyroid gland**
  - suppression
    - Loss of Supression in uremia

positive association of circulating FGF23 with PTH

Endothelial Damage



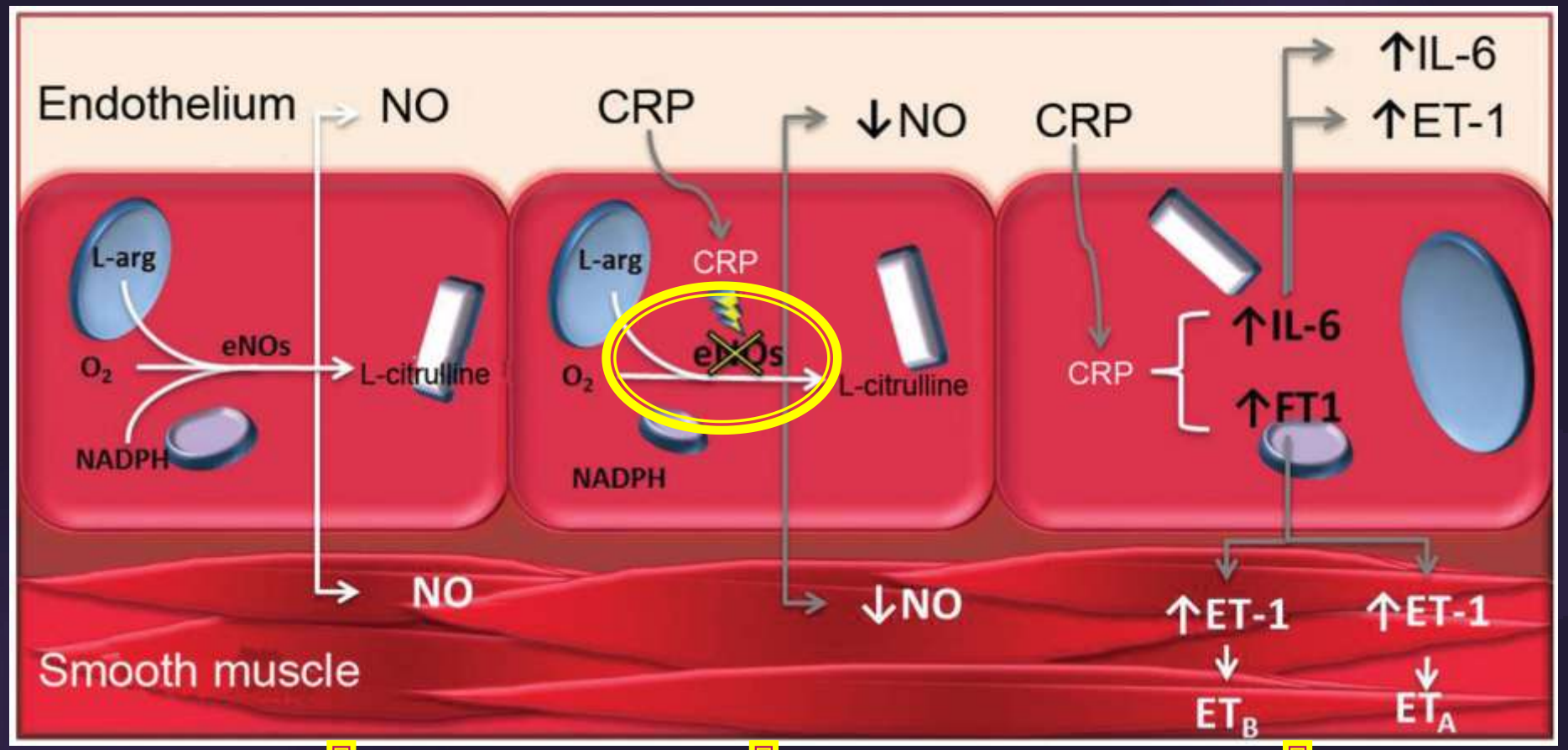
DNA methylation in atherosclerosis

monocytes differentiate into macrophages

gene-specific DNA methylation suggests alterations and advanced atherosclerotic lesions

toxic uraemic milieu may exert a crucial impact on epigenetic gene regulation and CKD-associated accelerated arteriosclerosis

Adam M. Zawada et al. Nephrol. Dial. Transplant. 2013



Promotes the proinflammatory milieu through ET1- and IL-6-release from endothelial cells

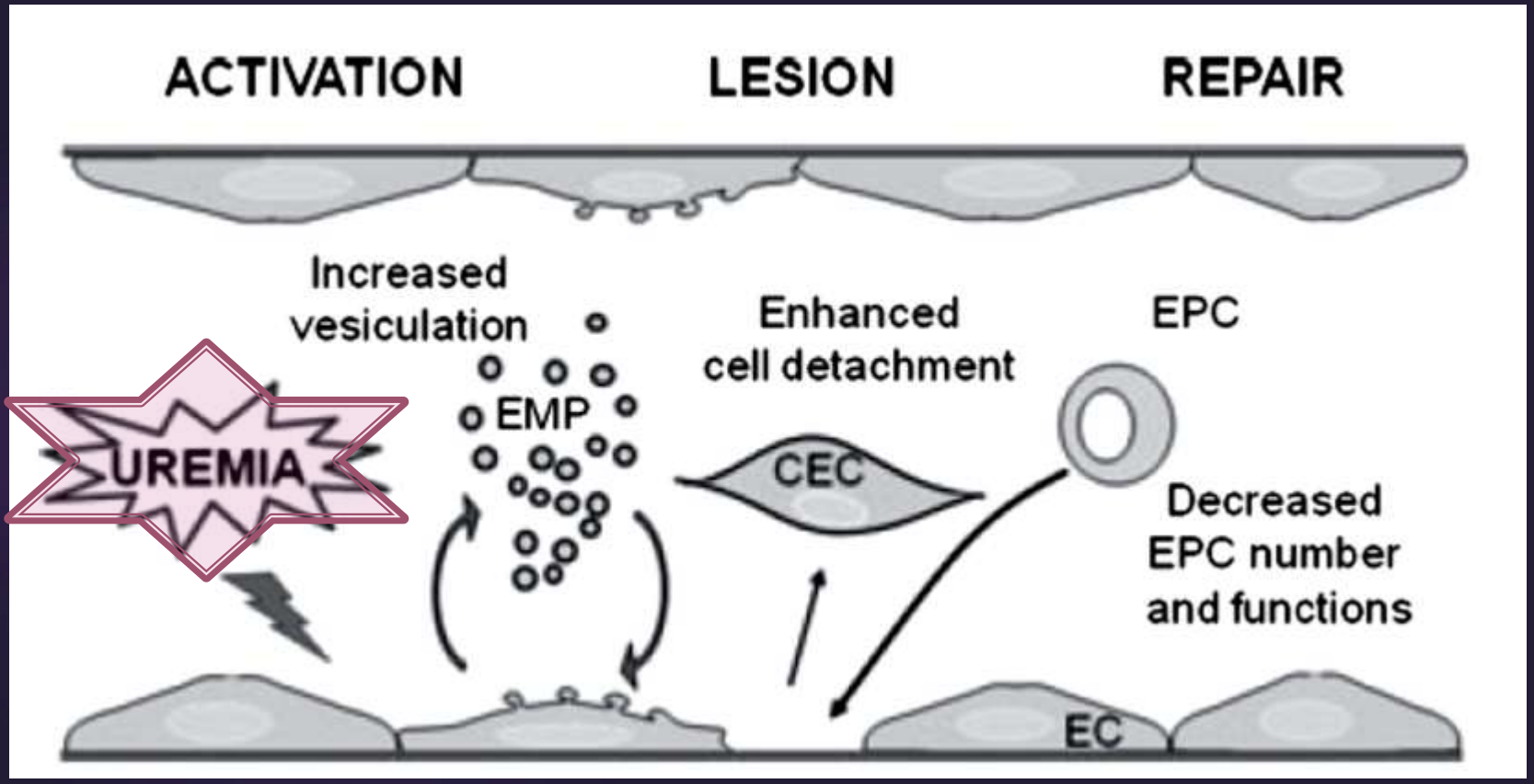
Adhesion and platelet activation increase when CRP is released by monocyte tissue factor

facilitating entrance of LDL into macrophages via MCP-1.

Circulating Endothelial Cells (CES)

BioMed Research International Volume 2014

- CEC counts are increased in diseases associated with a high degree of endothelial cell activation and/or injury



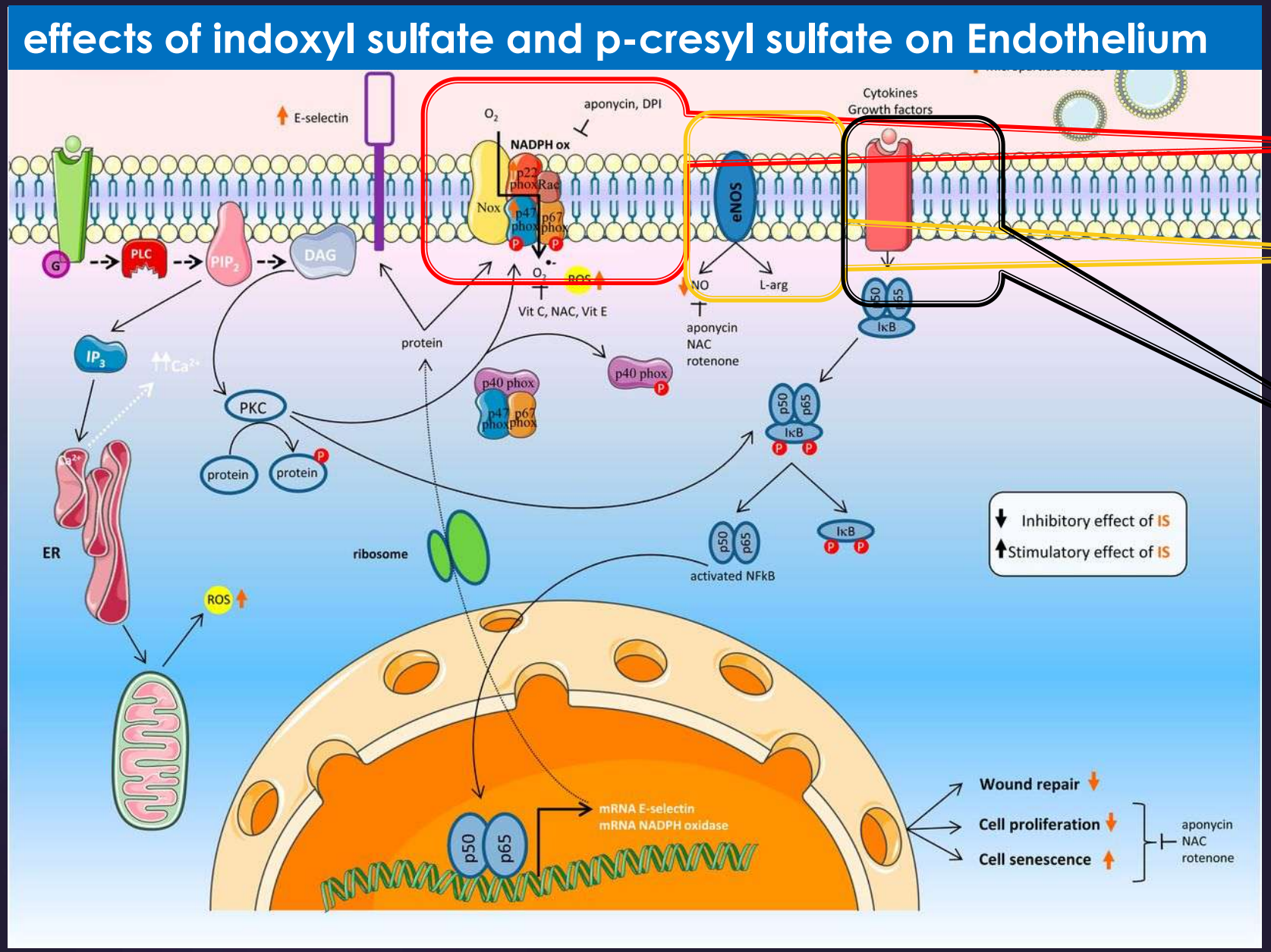
(1) Uremia induces the release of endothelial microparticles (EMP)

(2) increase in circulating endothelial cells (CEC)

(3) uremia impairs the survival of endothelial progenitor cells (EPC)

combination of different surface antigens such as CD146, CD45, and CD31 to detect the endothelial cells

effects of indoxyl sulfate and p-cresyl sulfate on Endothelium



NADPH ox excess ROS

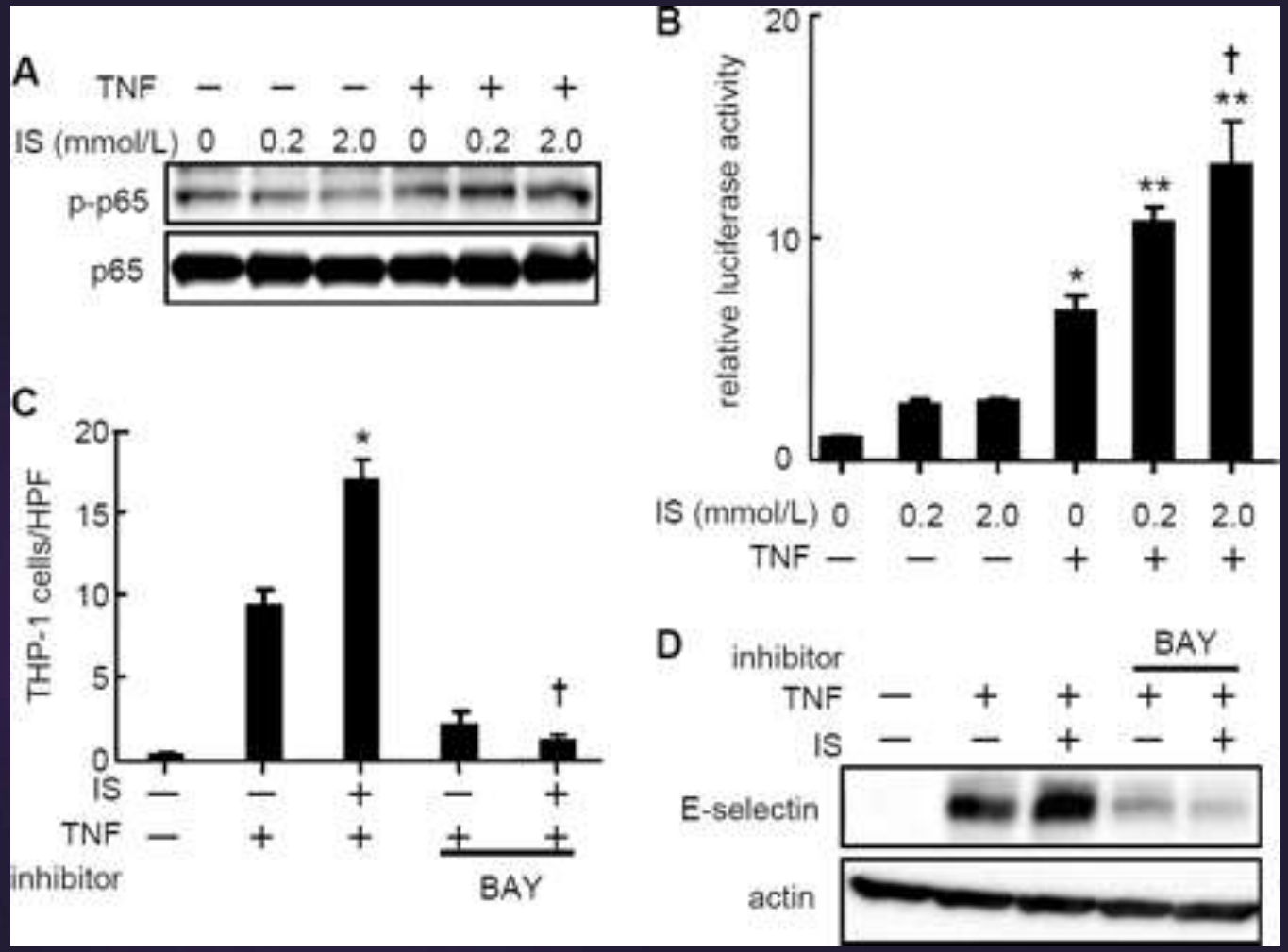
Inhibit eNO

Promote for Cytokine production

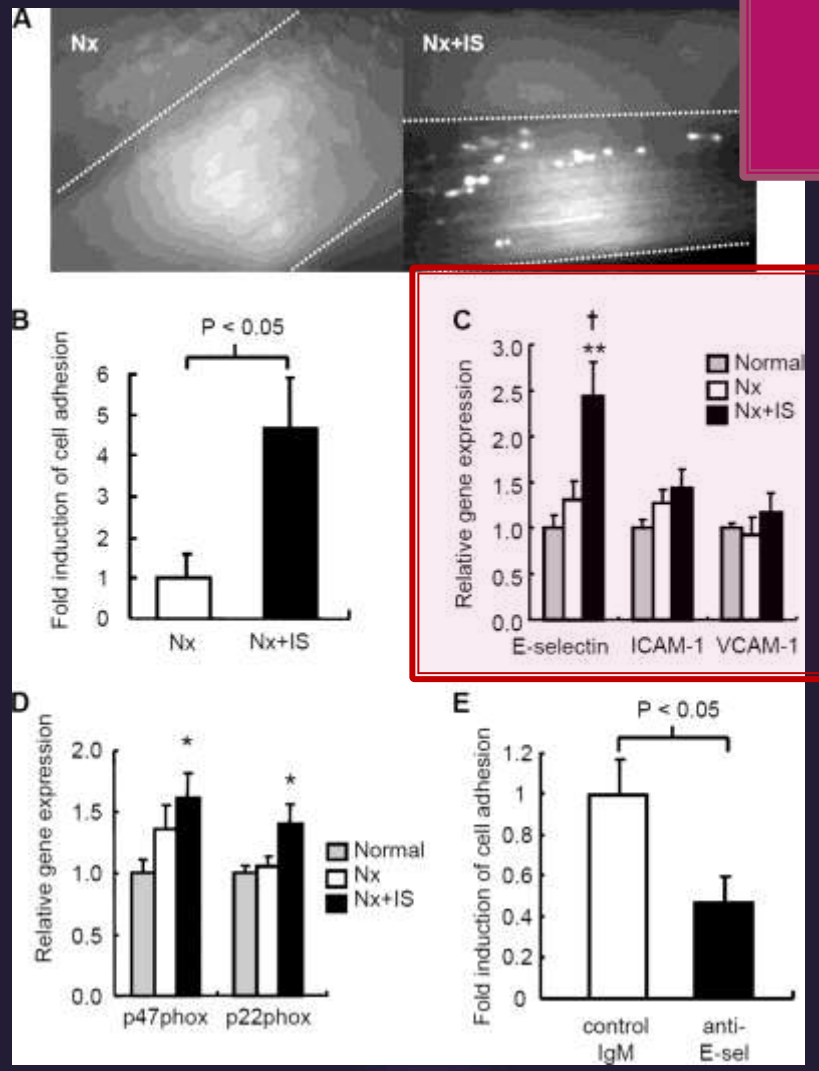
CELL SENSSCENSE

Raymond Vanholder et al. JASN , 2014

Indoxyl Sulfate Induces Leukocyte-Endothelial Interactions through Up-regulation of E-selectin , ICAM , VCAM and TNF α :Journal of Biological Chemistry ,Dec 2010



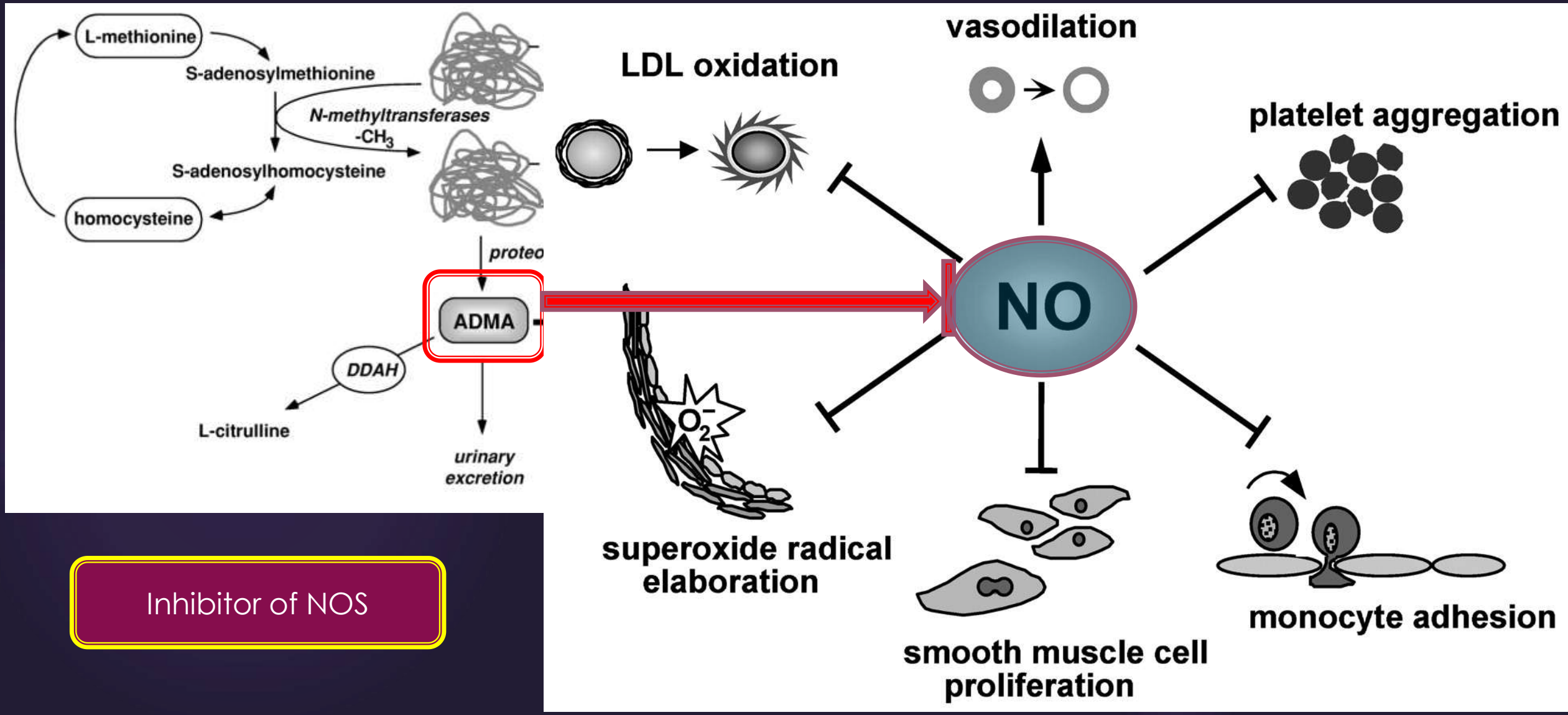
Effects of indoxyl sulfate on the TNF-α-induced NF-κB pathway



Nx: only water
Nx IS : IS

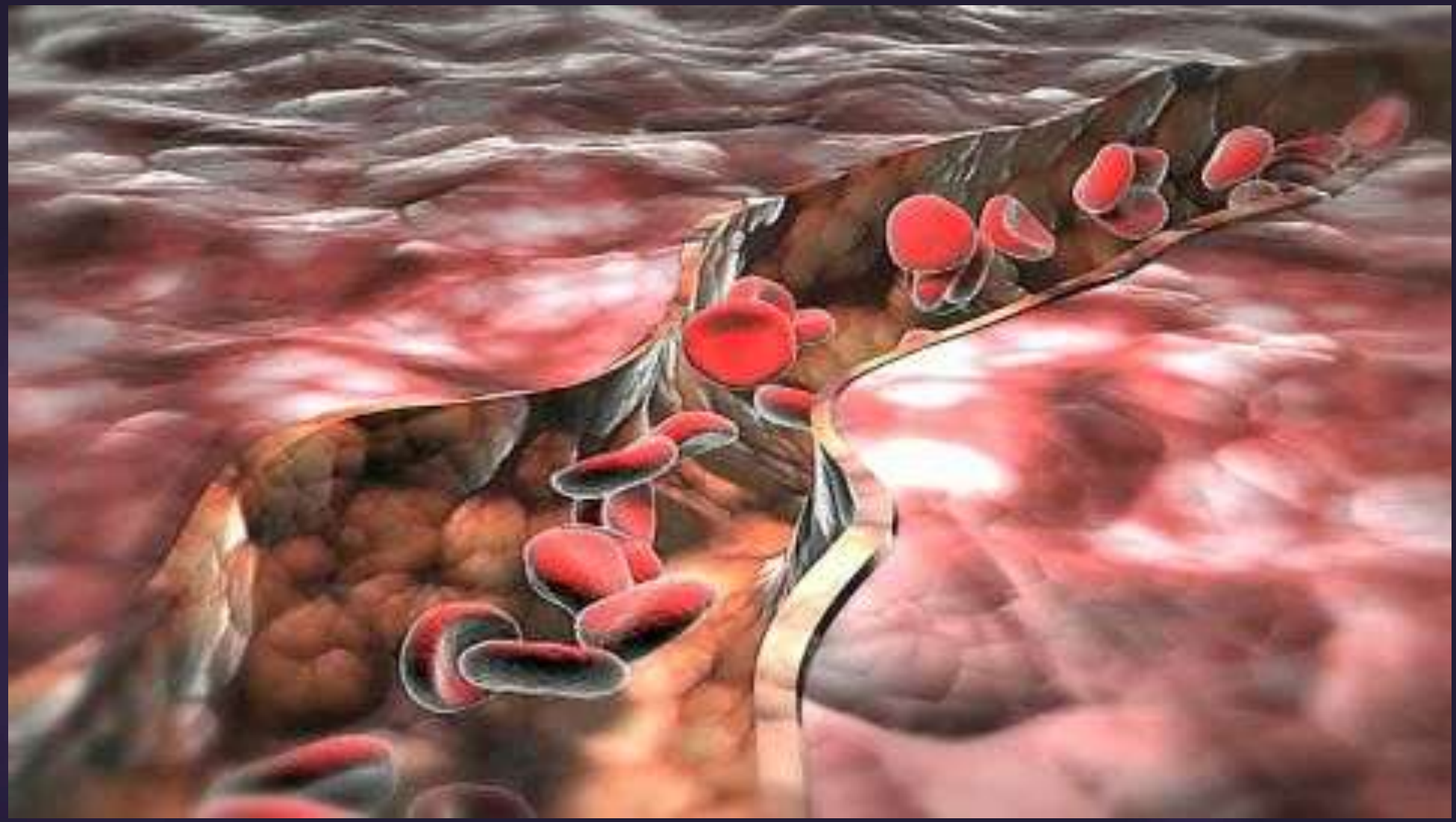
ADMA : PB Toxins Retention

J Am Soc Nephrol.
2015 Apr



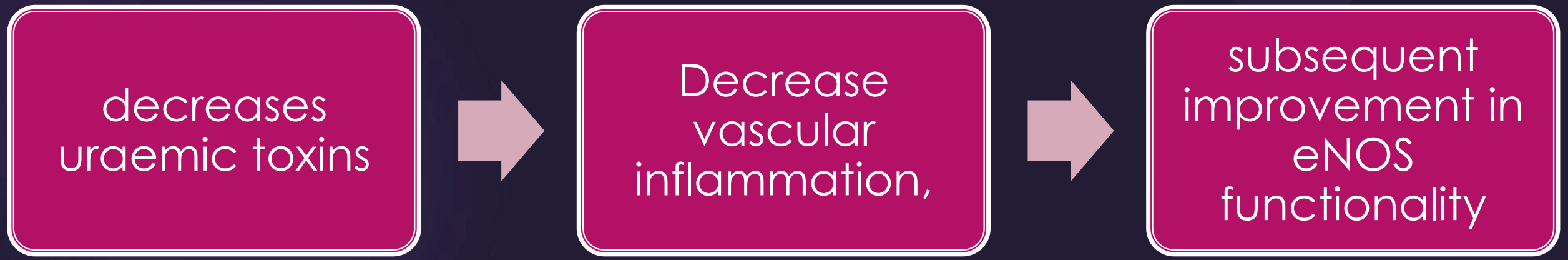
Inhibitor of NOS

HDF and Endothelial Functions



HDF and Endothelia Functions

High-efficiency on-line HDF prevents the endothelial dysfunction and stiffening of the conduit arteries in ESRD patients compared with high-flux HD Nephrol. Dial. Transplant. (2013)



HDF and Endothelia Functions

Therapeutic Apheresis and Dialysis

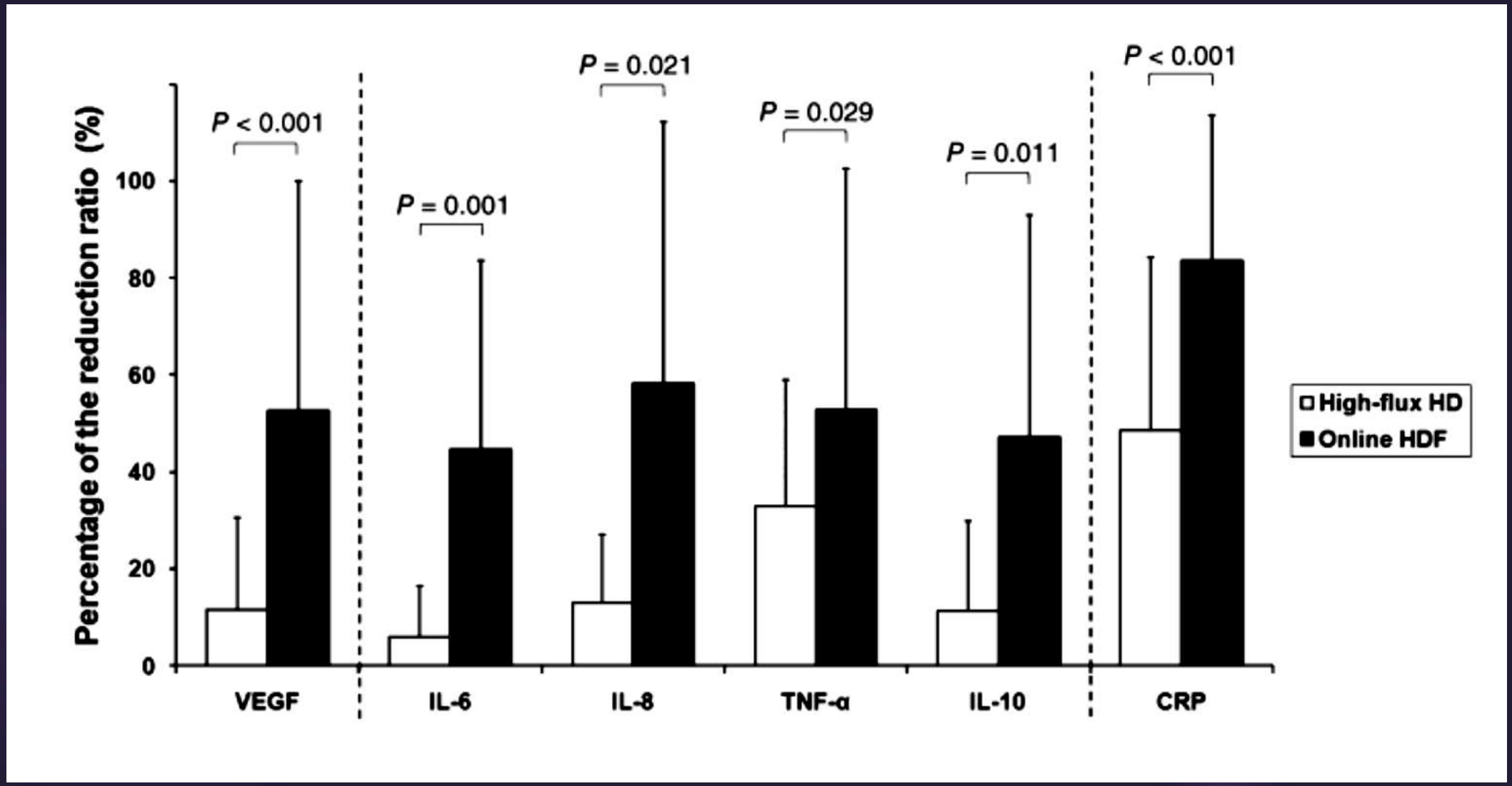
Therapeutic Apheresis and Dialysis 2013; 17(5):557–563
doi: 10.1111/1744-9987.12016

Enhanced Vascular Endothelial Growth Factor and Inflammatory Cytokine Removal With Online Hemodiafiltration Over High-Flux Hemodialysis in Sepsis-Related Acute Kidney Injury Patients

Wiwat Chancharoenthana,[1,2] Khajohn Tiranathanagul,[1,3] Nattachai Srisawat,[1,3] Paweena Susantitaphong,[1] Asada Leelahavanichkul,[4] Kearkiat Praditpornsilpa,[1] Kriang Tungsanga,[1] and Somchai Eiam-Ong[1]

HDF and inflammatory markers

Therapeutic Apheresis and Dialysis 2013; 17(5):557–56



Nephrol Dial Transplant (2008) 23: 2337–2343
doi: 10.1093/ndt/gfm951
Advance Access publication 27 February 2008

Original Article

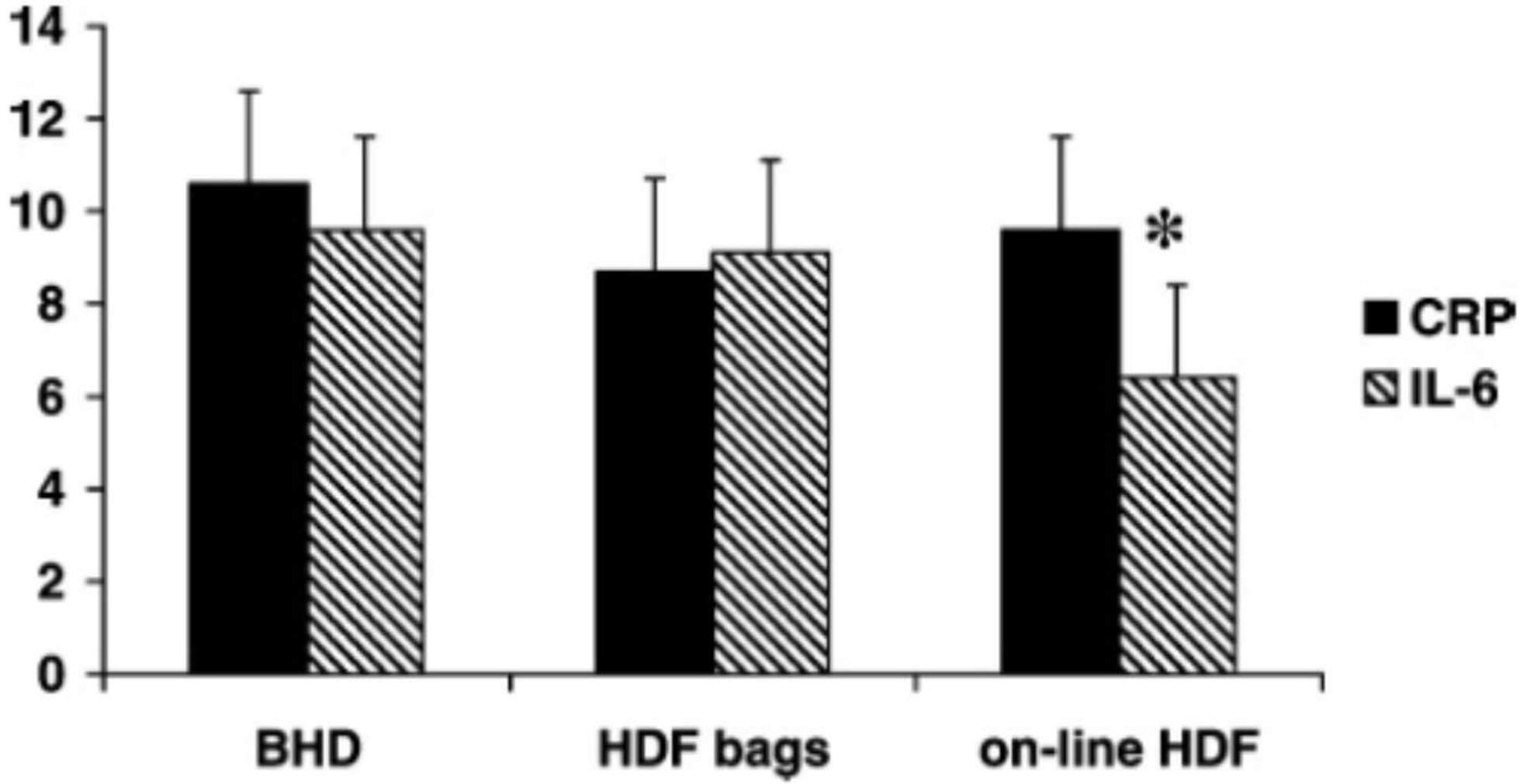
NDT
Nephrology Dialysis Transplantation

Chronic inflammation and mortality in haemodialysis: effect of different renal replacement therapies. Results from the RISCAVID study

Vincenzo Panichi[1], Giovanni M. Rizza[2], Sabrina Paoletti[1], Roberto Bigazzi[3], Mauro Aloisi[4], Giuliano Barsotti[1], Paolo Rindi[5], Giacli' Donati[2], Alessandro Antonelli[6], Erica Panicucci[1], Gianni Tripepi[7], Ciro Tetta[8] and Roberto Palla[9] on behalf of the RISCAVID Study Group[10]

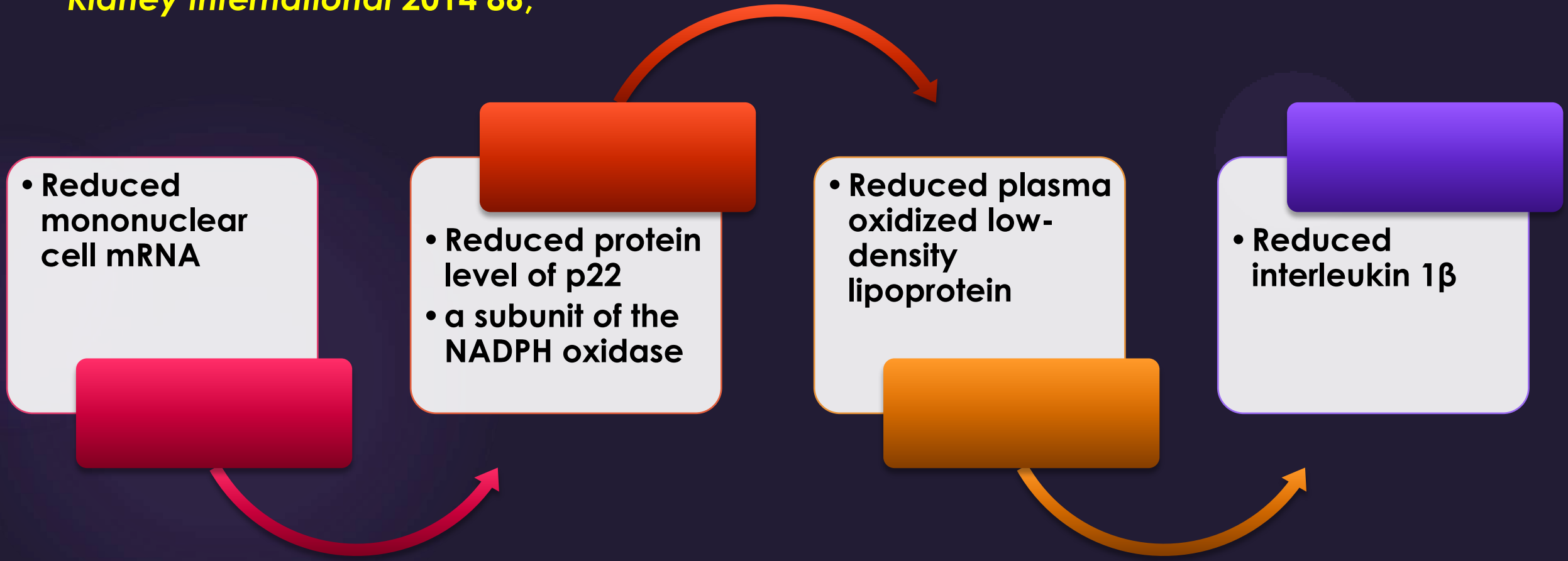
RISCAVID, a prospective, observational study on 757 prevalent patients with a 30-month follow-up

IL-6 but not CRP was statistically reduced in online HDF versus BHD and HDF ($P < 0.01$).

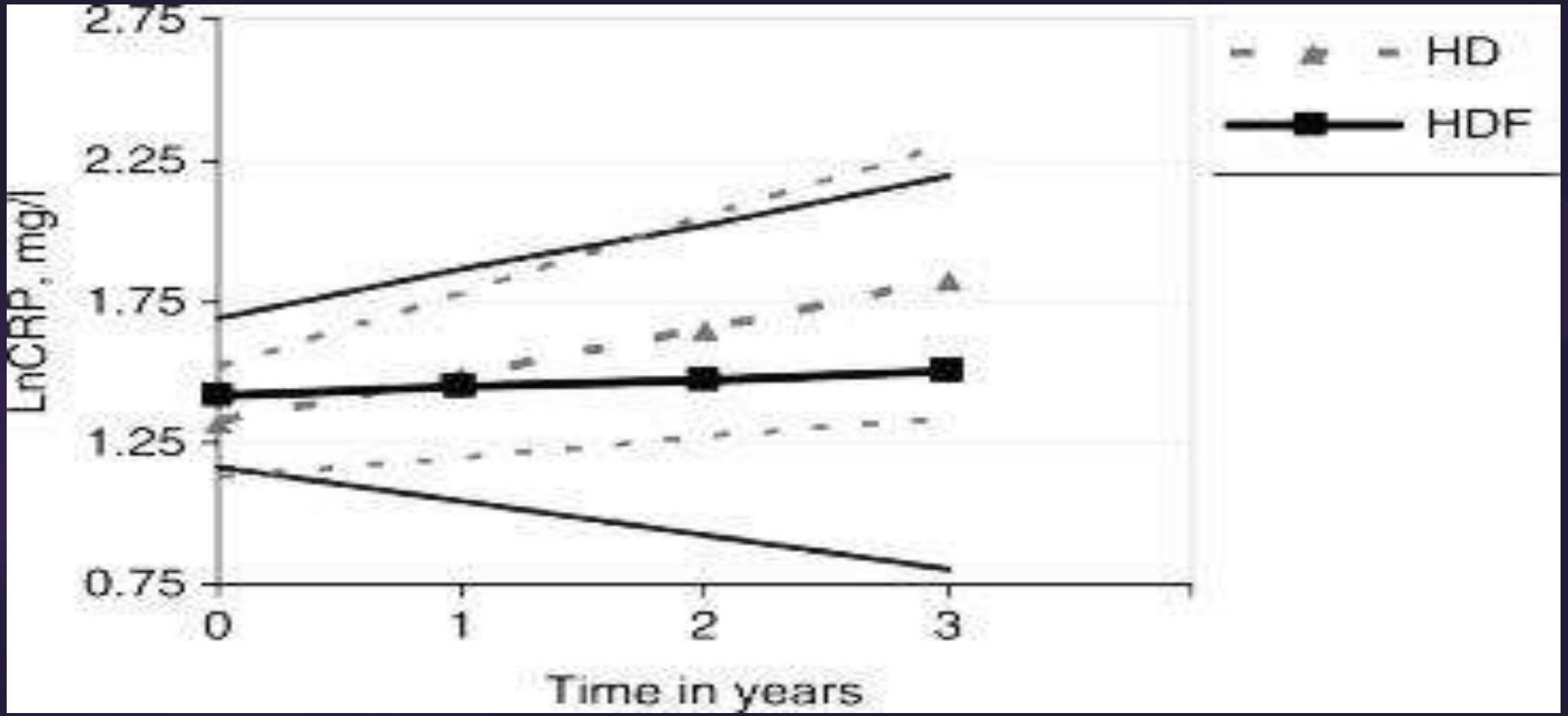


HDF against LF HD and reduction of inflammation

***Kidney International* 2014 86,**



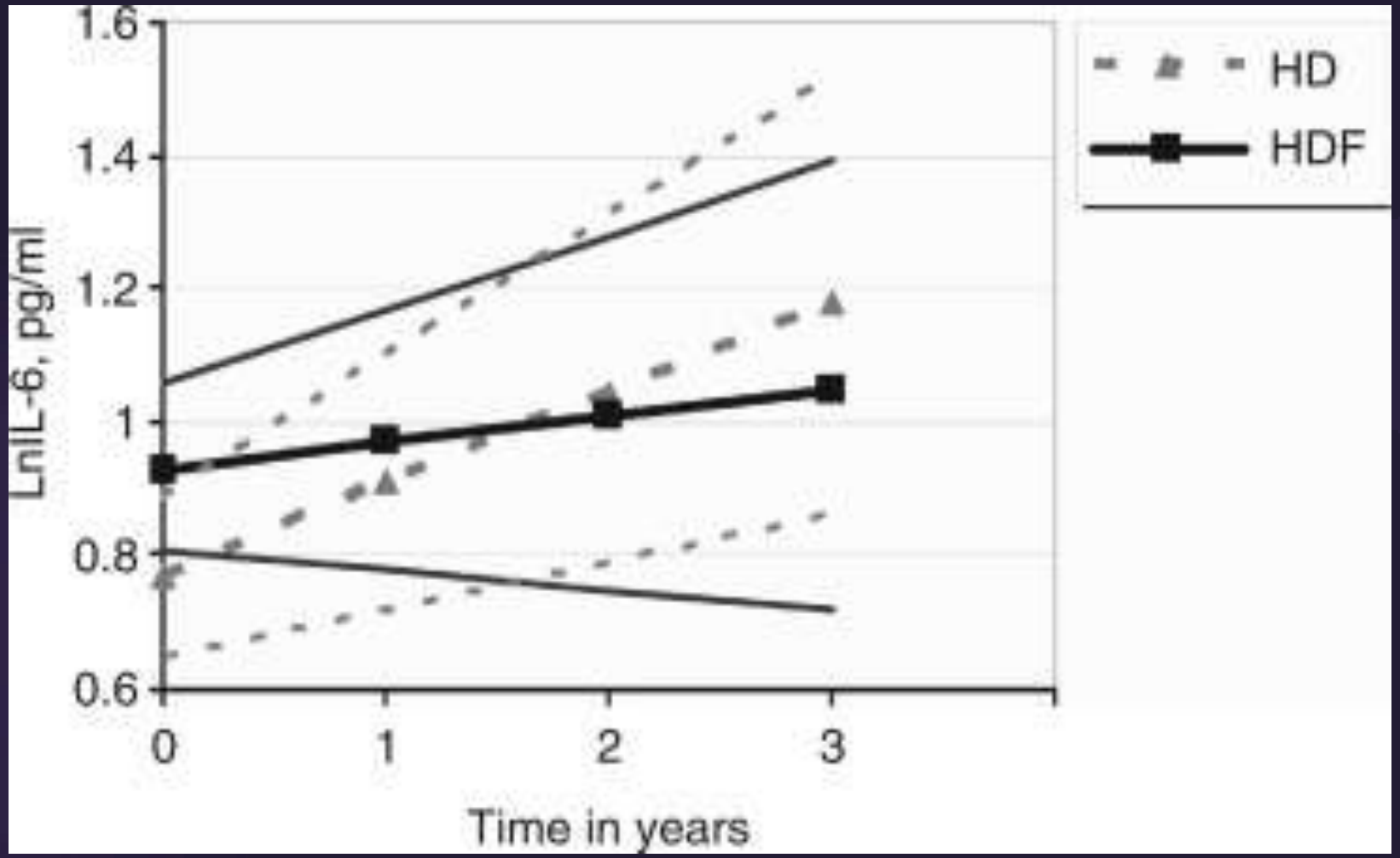
HDF and CRP (measured for up to 3 years in 405 patients)



Kidney International **2014 86,**

Mean changes with 95% confidence intervals. Estimates derived from linear mixed-effects model

HDF and IL-6 (measured for up to 3 years in 405 patients)



Mean changes with 95% confidence intervals. Estimates derived from linear mixed-effects model

Kidney International 2014 86,

HDF and Endothelia Functions versus HF dialysis

- OLHDF improved endothelial dysfunction
- decrease in the number of endothelial microparticles (EMP)
- increase in the percentage of endothelial progenitor cells (EPC)

More players to come

Sclerostin

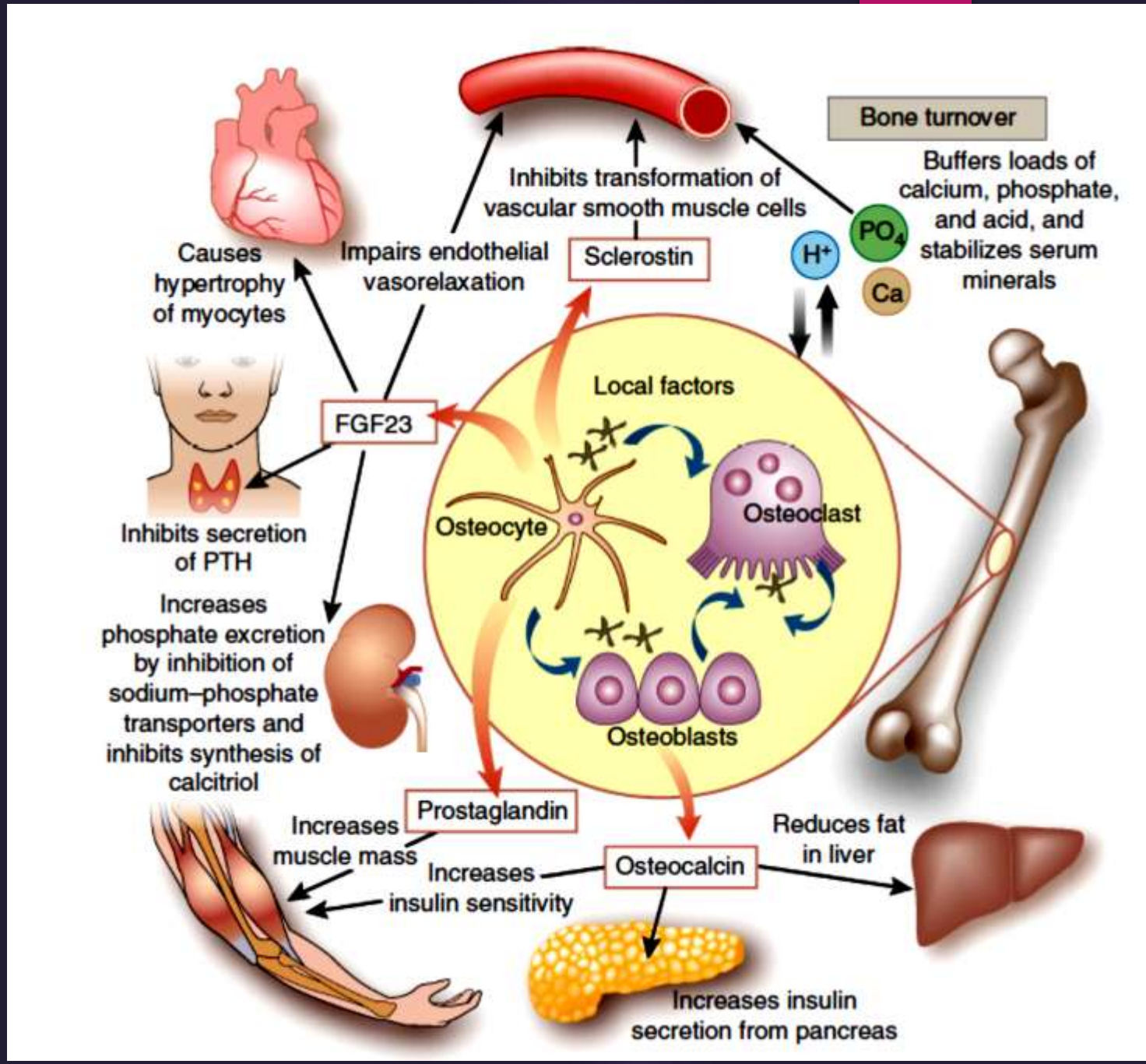
NEWS
European Renal Association -
European Dialysis and Transplant Association

Circulating Sclerostin: A New Parameter of Cardiovascular Risk in CKD-Patients

2 February 2015

Chronic Kidney Disease (CKD) is an important risk factor for cardiovascular disease. A significantly higher cardiovascular risk has even been identified for minor renal dysfunction [1] – and dialysis patients are at a very high risk: it is well known that the cardiovascular risk of patients with End Stage Renal Disease (ESRD) is increased about 20- to 30-fold compared to people with normal kidney function [2].

sclerostin can suppress the transformation of vascular smooth muscle cells into osteoblast-like cells.



Osteoprotegerin and sclerostin in chronic kidney disease prior to dialysis: potential partners in vascular calcifications

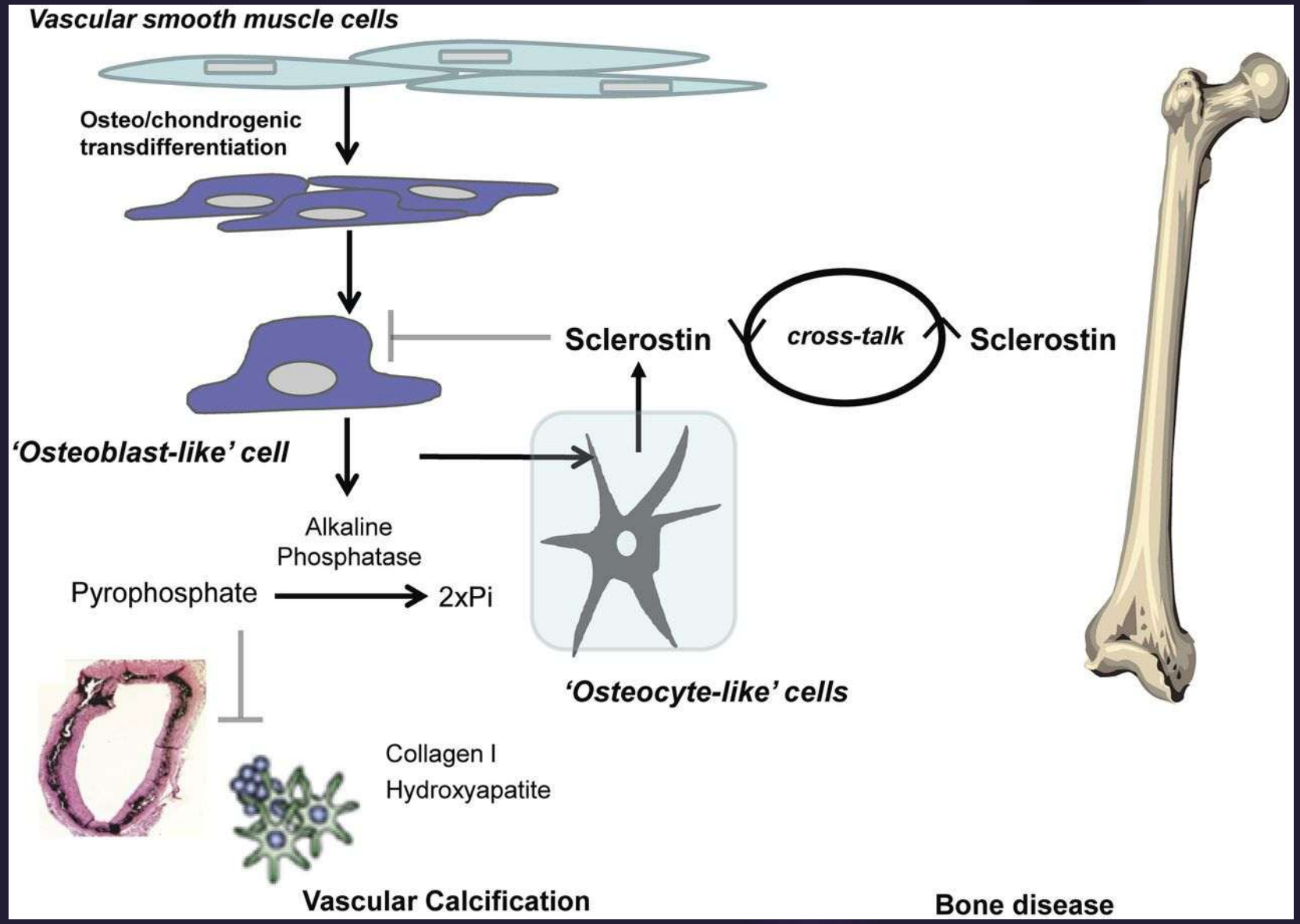
Nephrol. Dial. Transplant. (2015)

Evolution of bone and mineral metabolism markers with decline of kidney function

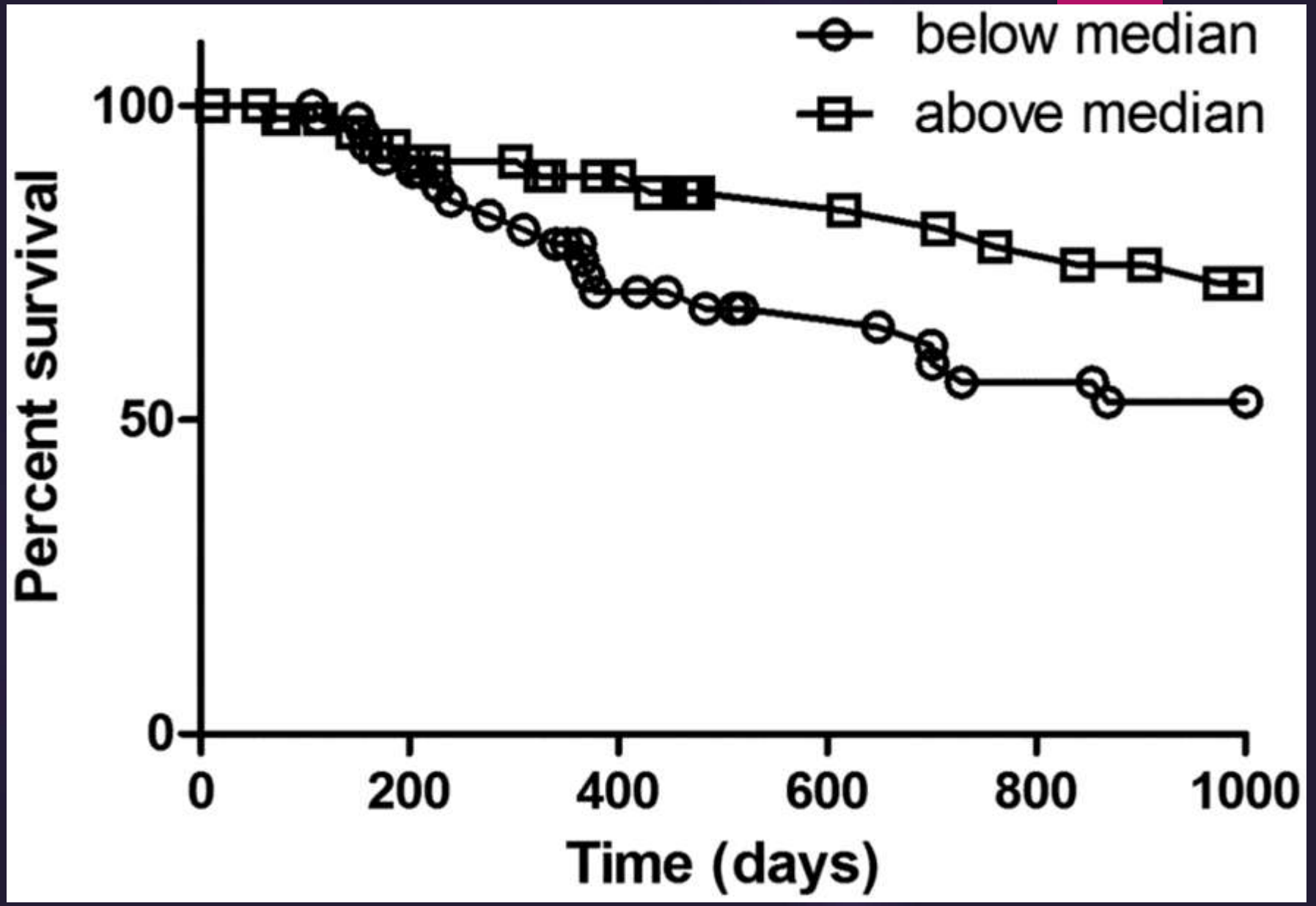
Parameter	CKD stage 1+2	CKD stage 5	P-value
PO_4 (mmol/L)	0.935 [0.580–1.410]	1.235 [1.020–2.340]	<0.0001
iPTH (pg/mL)	28.5 [10.0–90.0]	135.5 [20.0–493.0]	<0.0001
OPG (pmol/L)	5.20 [1.81–11.32]	9.86 [4.16–26.89]	<0.0001
Sclerostin (ng/mL)	0.655 [0.325–1.226]	1.046 [0.581–2.928]	<0.0001

Sclerostin cross talk

block the Wnt pathway in order to reduce the mineralization in the vascular tissue.
Sclerostin may spill over to the circulation and may reciprocally inhibit bone metabolism



Sclerostin: another bone-related protein related to all-cause mortality in haemodialysis?

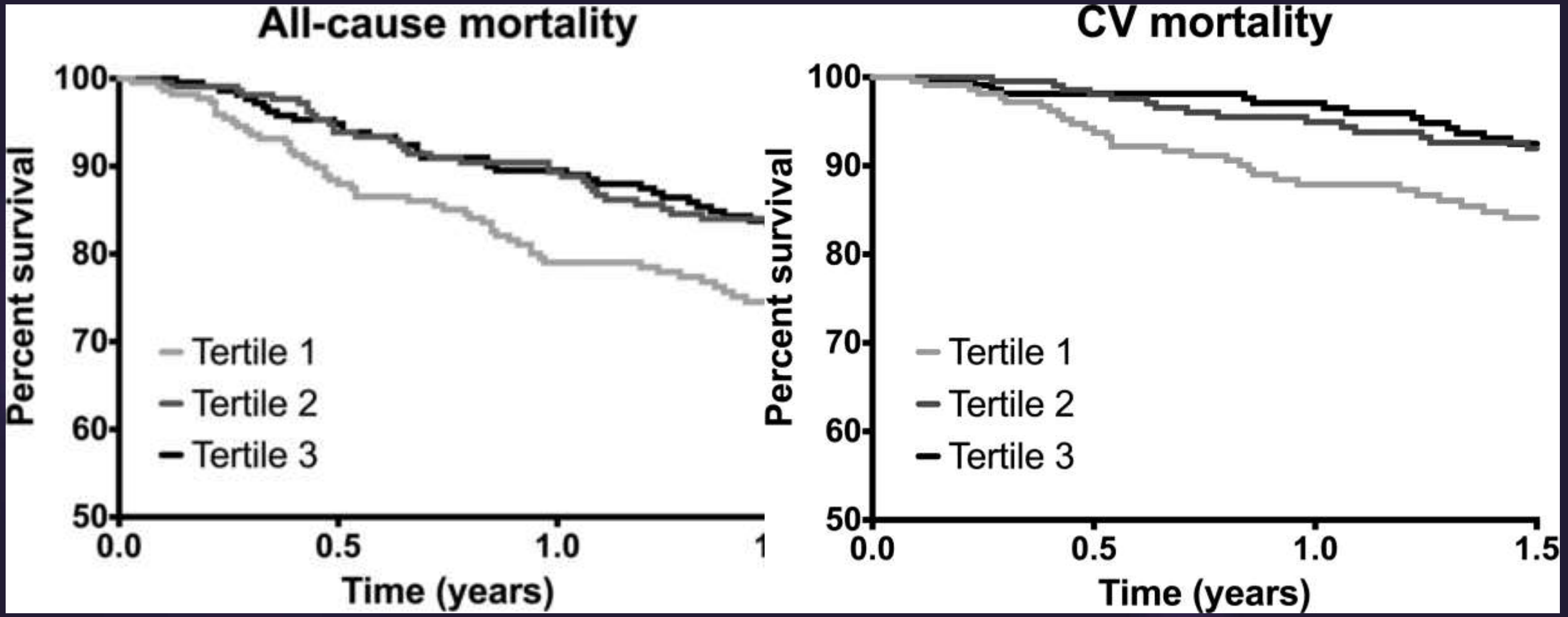


Liesbeth Viaene et al. Nephrol. Dial. Transplant. 2013

NDT
Nephrology Dialysis Transplantation

high levels of circulating sclerostin at 3 months after dialysis start were strongly associated with short-term cardiovascular survival over 18 months in dialysis patients

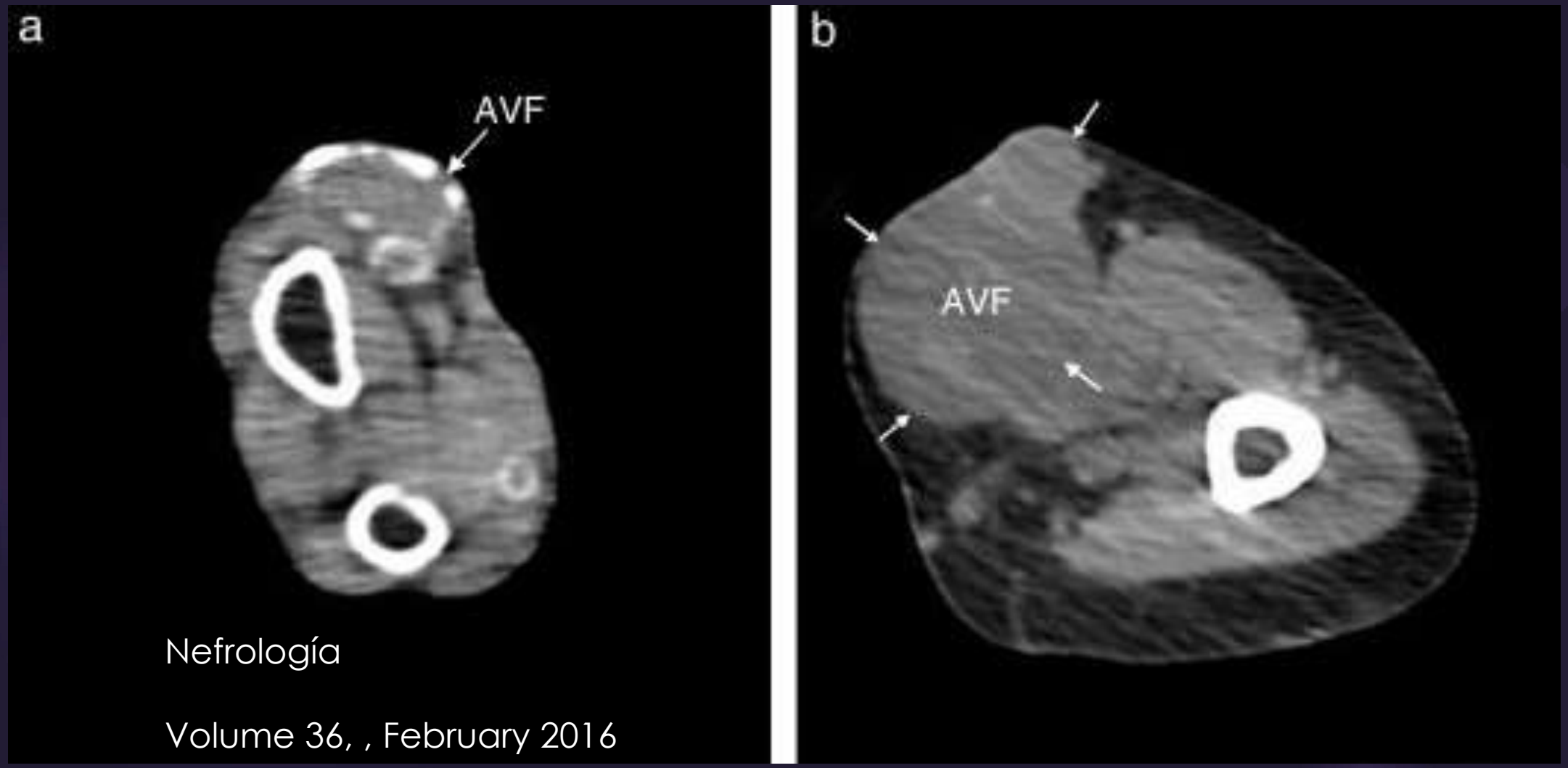
Nephrol. Dial. Transplant. (2015) 30



Kidney International (2015) 87

- In CKD patients serum sclerostin is elevated, and a recent study showed that **it could be produced ectopically in calcified aortic valves**.
- It is not clear whether this is a protective mechanism or whether the sclerostin is **just a marker of the terminal transformation of the vascular cells.**

AVF calcification Age , Albumin and S Scelorstin are predictors of AVF calcification



Nefrología

Volume 36, , February 2016

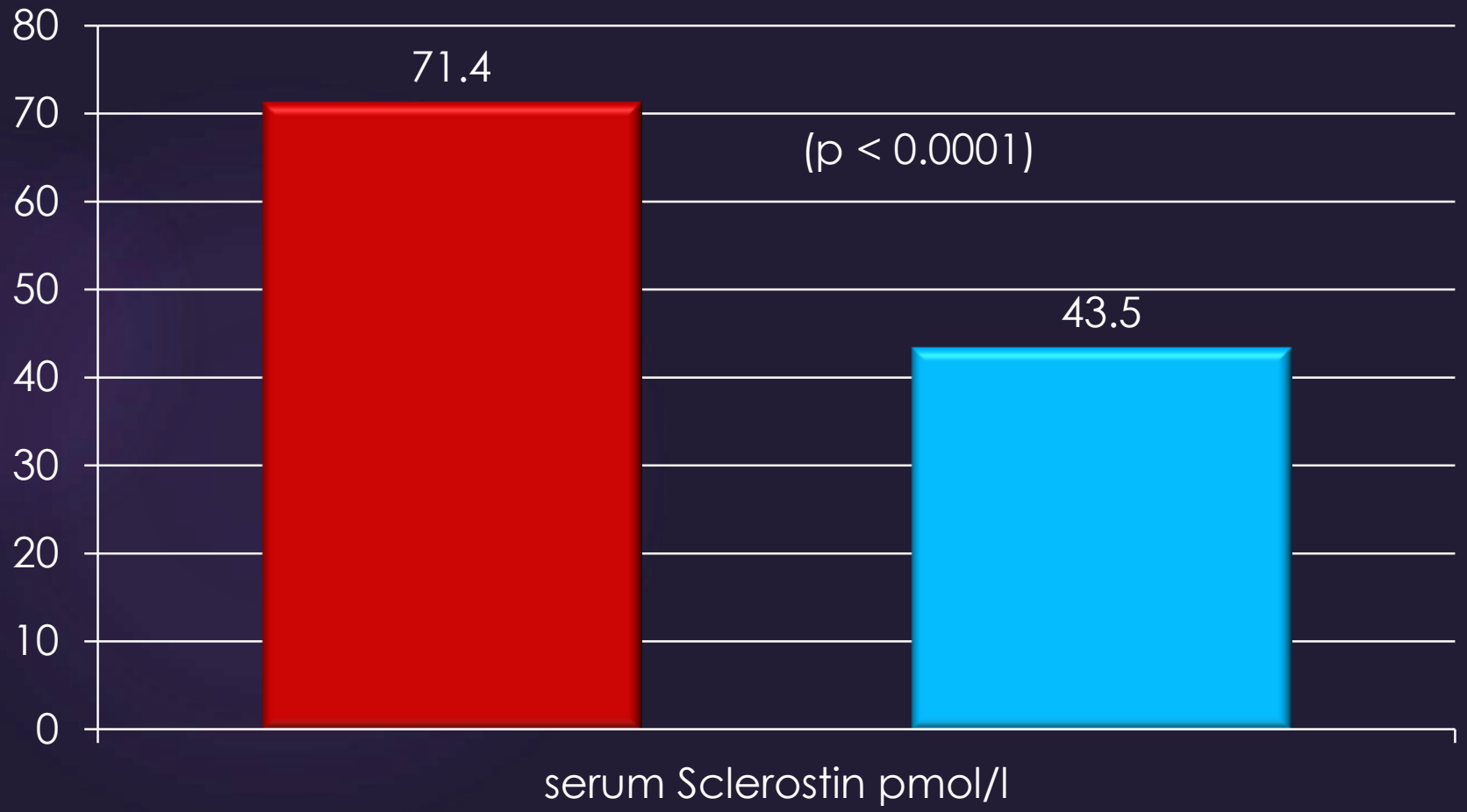
- Significantly higher sclerostin levels were found in the serum of patients with epigastric and coronary artery calcification (calcification score 100 or more).

Kidney International advance online publication, 2 September 2015

Sclerostin Declines during Hemodialysis and Appears in Dialysate

Vol. 38, No. 1, 2014

Blood Purification



Higher Kt/V correlated with greater relative decrease of sclerostin (r = 0.467; p = 0.001).

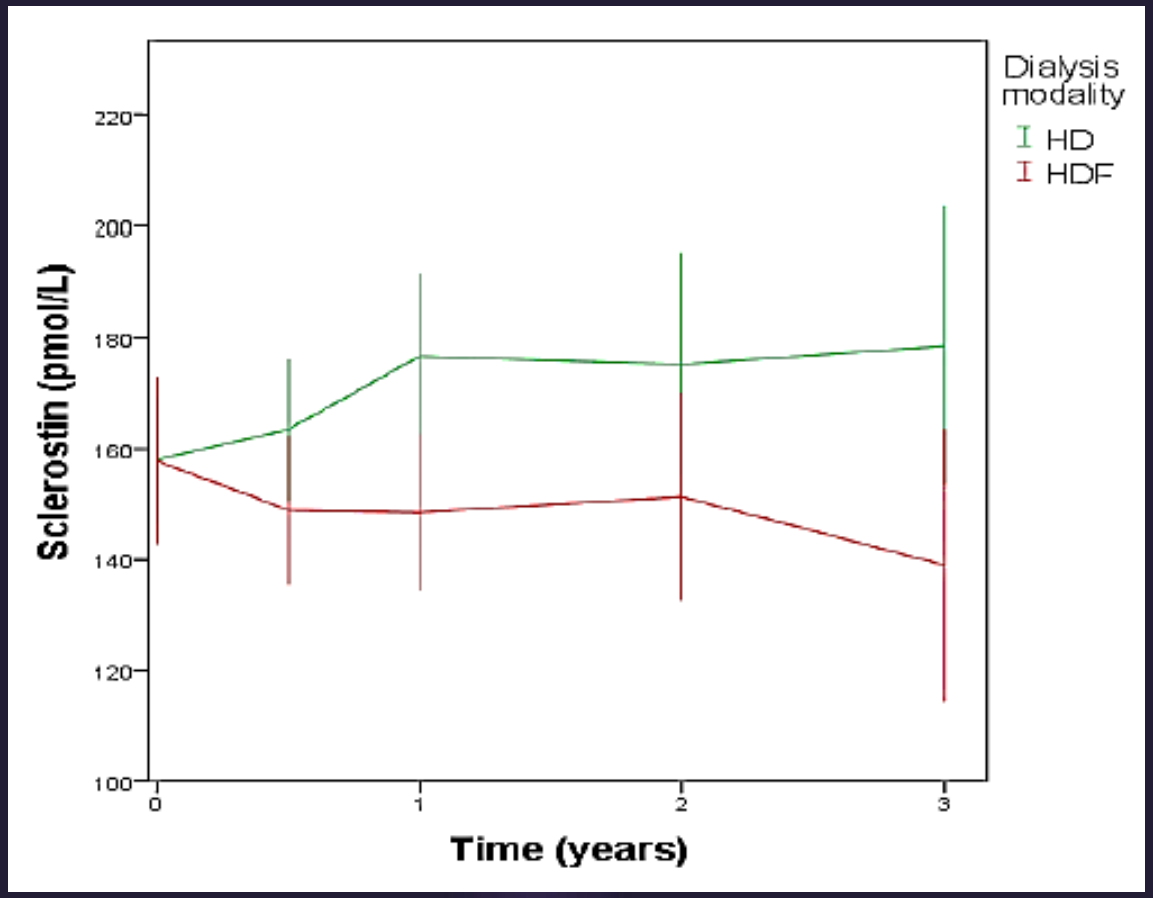
with online hemodiafiltration

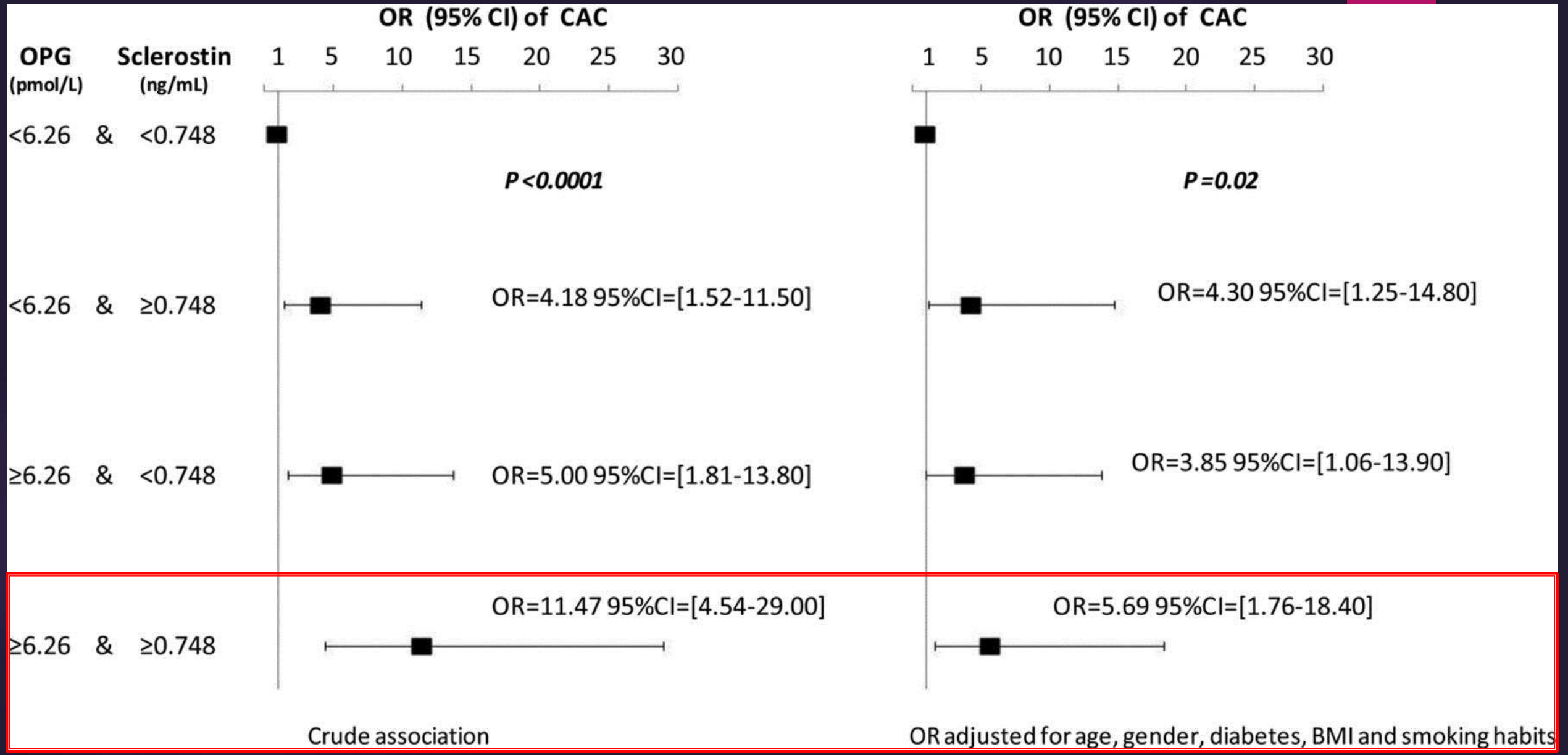
Camiel de Roij van Zuijdewijn,[1,2] Lotte Lips,[1] Muriel Grooteman,[1,2] Marc Vervloet,[1,2] Menso Nubé[1,2], Peter Blankestijn[3], René van den Dorpel,[4] Denis Fouque,[5] Solenne Pelletier,[5] Michiel Bots[6] and Piet ter Wee[1,2]

[1]Department of Nephrology, [2]Institute for Cardiovascular Research (ICaR-VU), VU University Medical Center, Amsterdam, the Netherlands; [3]Department of Nephrology, [5]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, the Netherlands; [4]Department of Internal Medicine, Maasstad Hospital, Rotterdam, the Netherlands; [5]Nephrology, Centre Hospitalier Universitaire de Lyon, Pierre Benite, France

Contrast
CONvective TRAnsport STudy

Characteristic	Entire cohort (n=714)	Analyzed patients (n=396)
Age (yrs)	64.1 (13.7)	63.6 (13.9)
Gender (male)	445 (62.3%)	244 (61.6%)
BMI (kg/m²)	25.4 (4.8)	25.0 (4.8)
RKF (>100mL/24h)	376 (52.7%)	223 (56.3%)
Dialysis vintage (yrs)	2.0 (1.0-4.0)	1.8 (0.9-3.3)
Kt/V	1.40 (0.22)	1.38 (0.21)
Albumin (g/L)	40.4 (3.8)	40.0 (4.0)
PTH (pmol/L)	20 (10-35)	21 (11-36)
Assigned to HDF	358 (50.1%)	198 (50.0%)

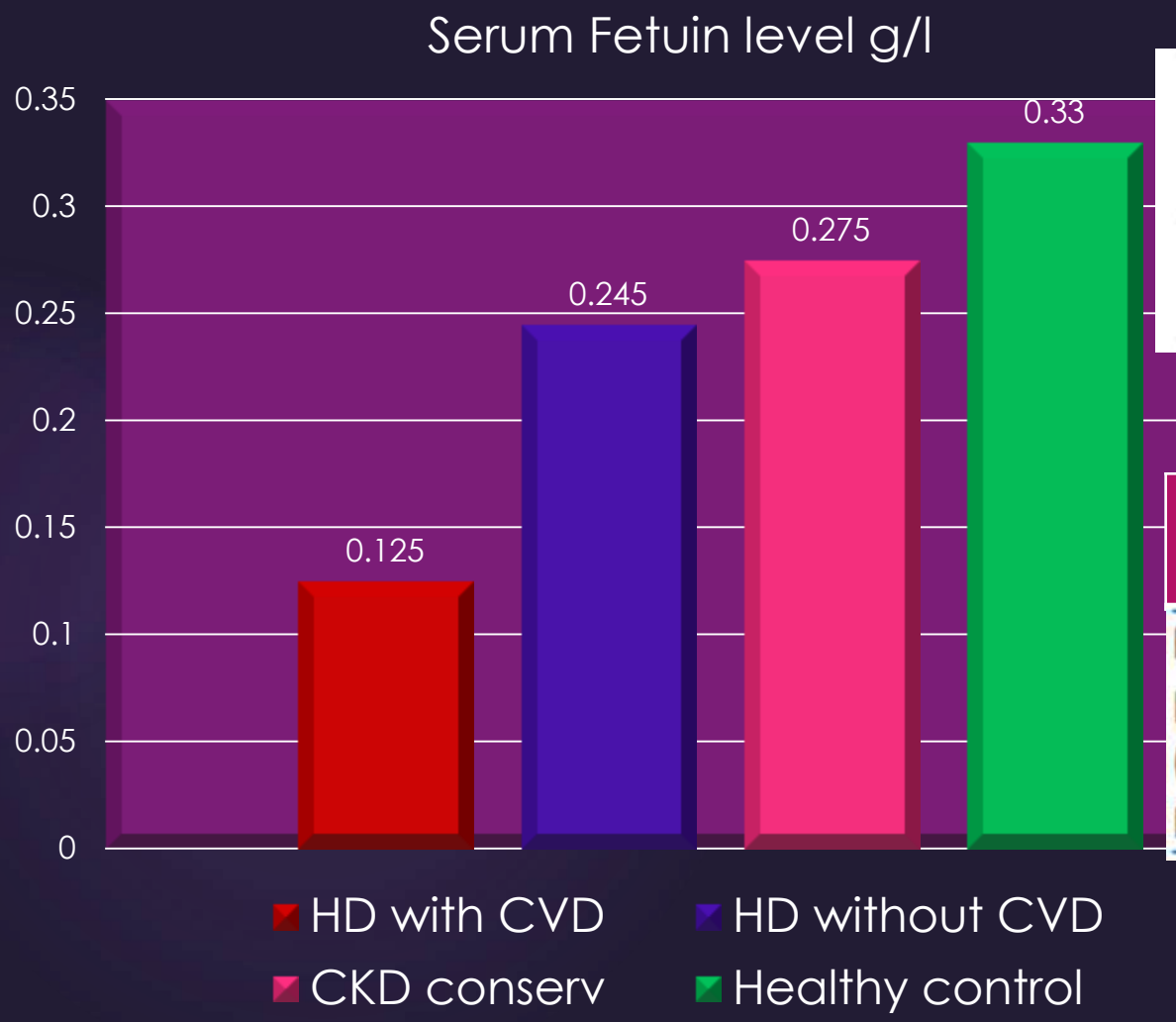




A logistic regression model clearly showed that the risk to present CAC was significantly increased when both OPG (≥6.26 pmol/L) and sclerostin (≥0.748 ng/mL) levels were high *Nephrol. Dial. Transplant. (2015)*

Fetuin Level in CKD patients

Elsayed.H etal Actamedica jan 2015



Parameter	ESRD with CVD		ESRD without CVD		CKD	
	r	p	r	p	r	p
hs-CRP (mg/L)	−0.010	<0.05	−0.087	<0.05	0.164	>0.05
Homocysteine (μmol/L)	−0.045	<0.05	−0.450	<0.05	0.228	>0.05

	HD - CVD		HD without CVD		CKD	
hs-CRP (mg/L)	10.4*	<0.001	18.44*	<0.001	−0.04*	>0.05
Homocysteine (μmol/L)	7.724	<0.001	7.939	<0.01	4.641	>0.05
Fetuin-A (g/L)	−6.23	<0.001	-2.22	<0.05	−1.22	>0.05

CKD on HD and conservative treatment against Healthy control

HD and PTH level

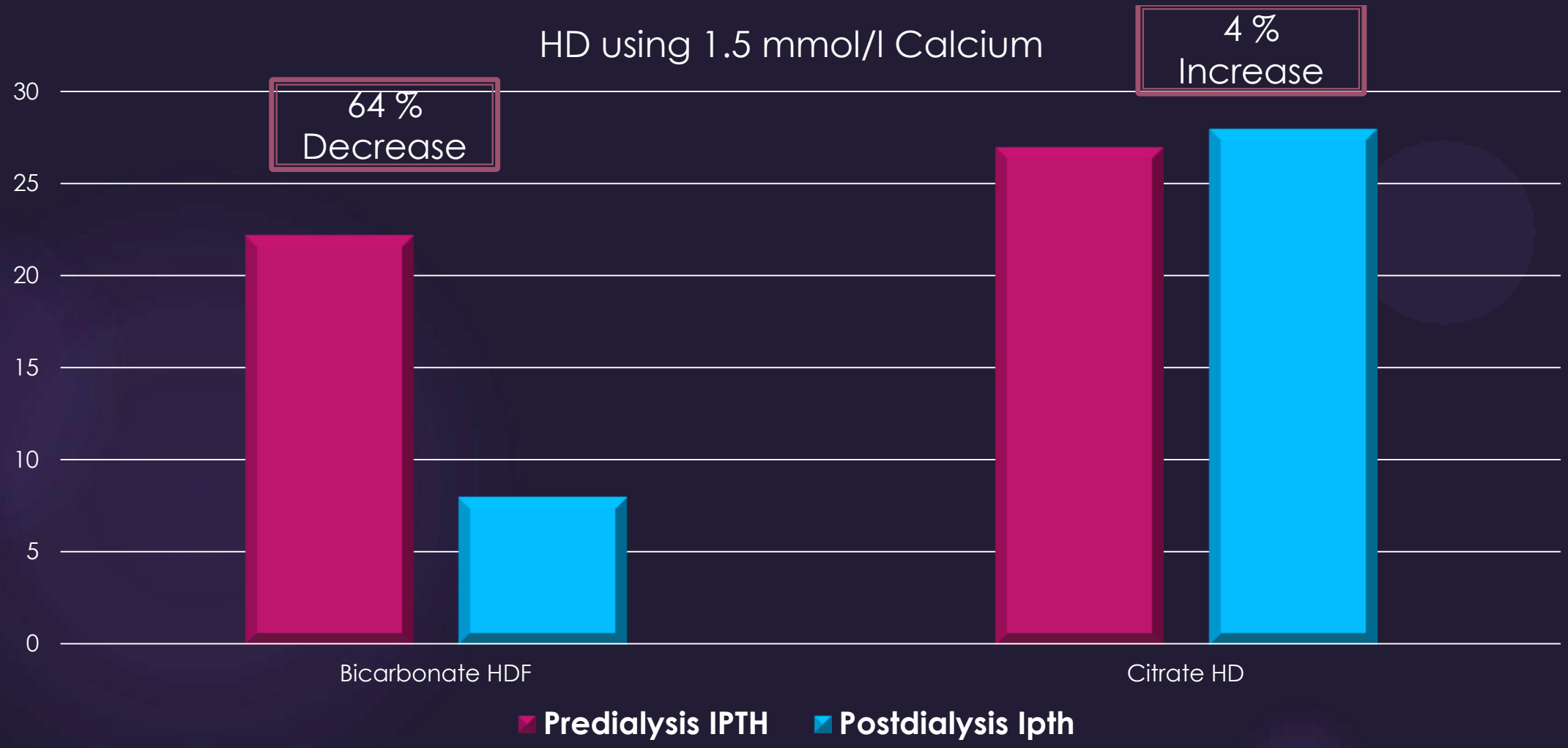
- parathyroid tissue is sensitive to immediate calcium load.

- Changes of PTH during procedure negatively correlated significantly with serum Ca2+ changes

Kidney Blood Press Res 2015;40

iPTH changes with different buffer use

Kidney Blood Press Res 2015;40



NDT Advance Access published May 9, 2011

Nephrol Dial Transplant (2011) 0: 1–6
doi: 10.1093/ndt/gfr179

Original Article

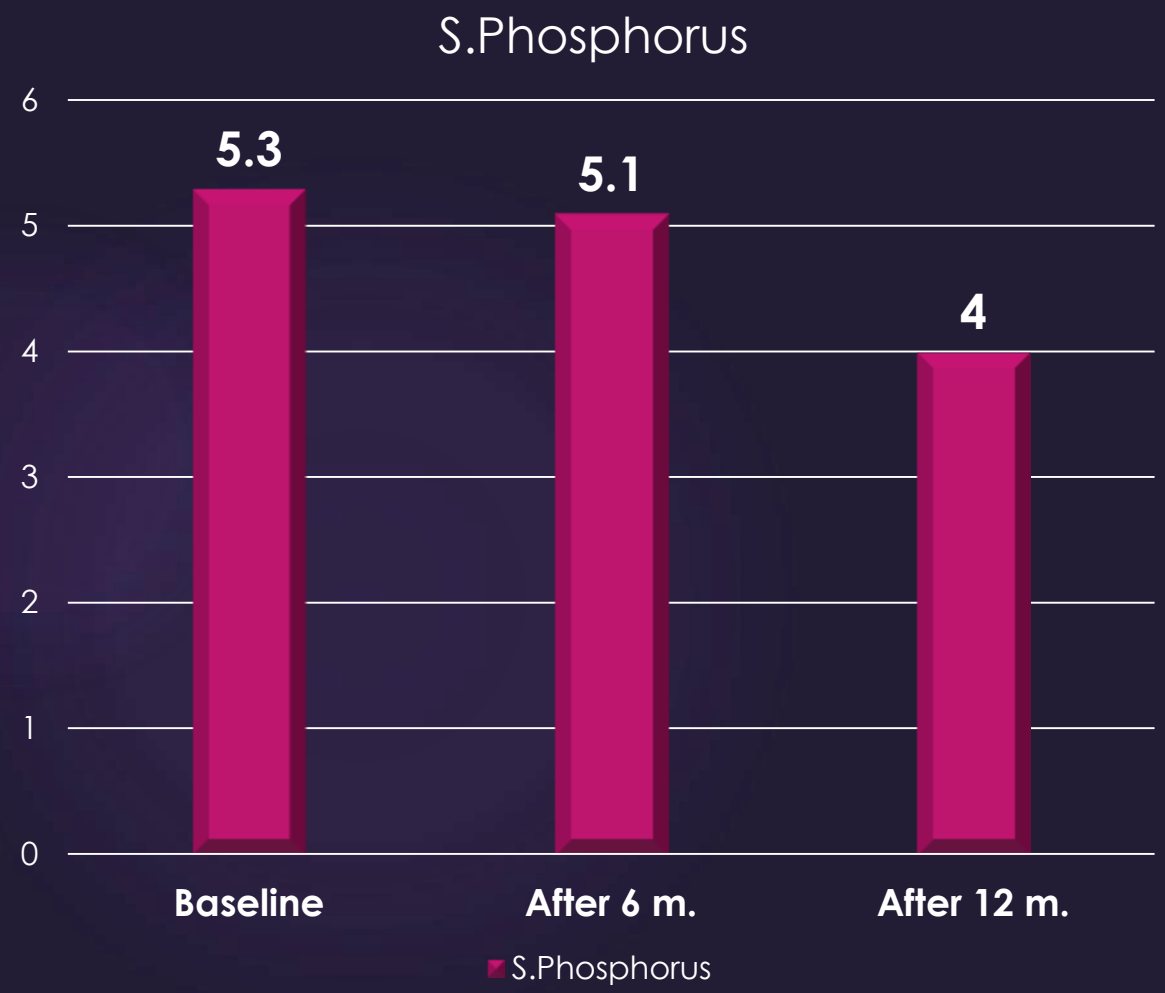
Effect of post-dilutional on-line haemodiafiltration on serum calcium, phosphate and parathyroid hormone concentrations in uraemic patients

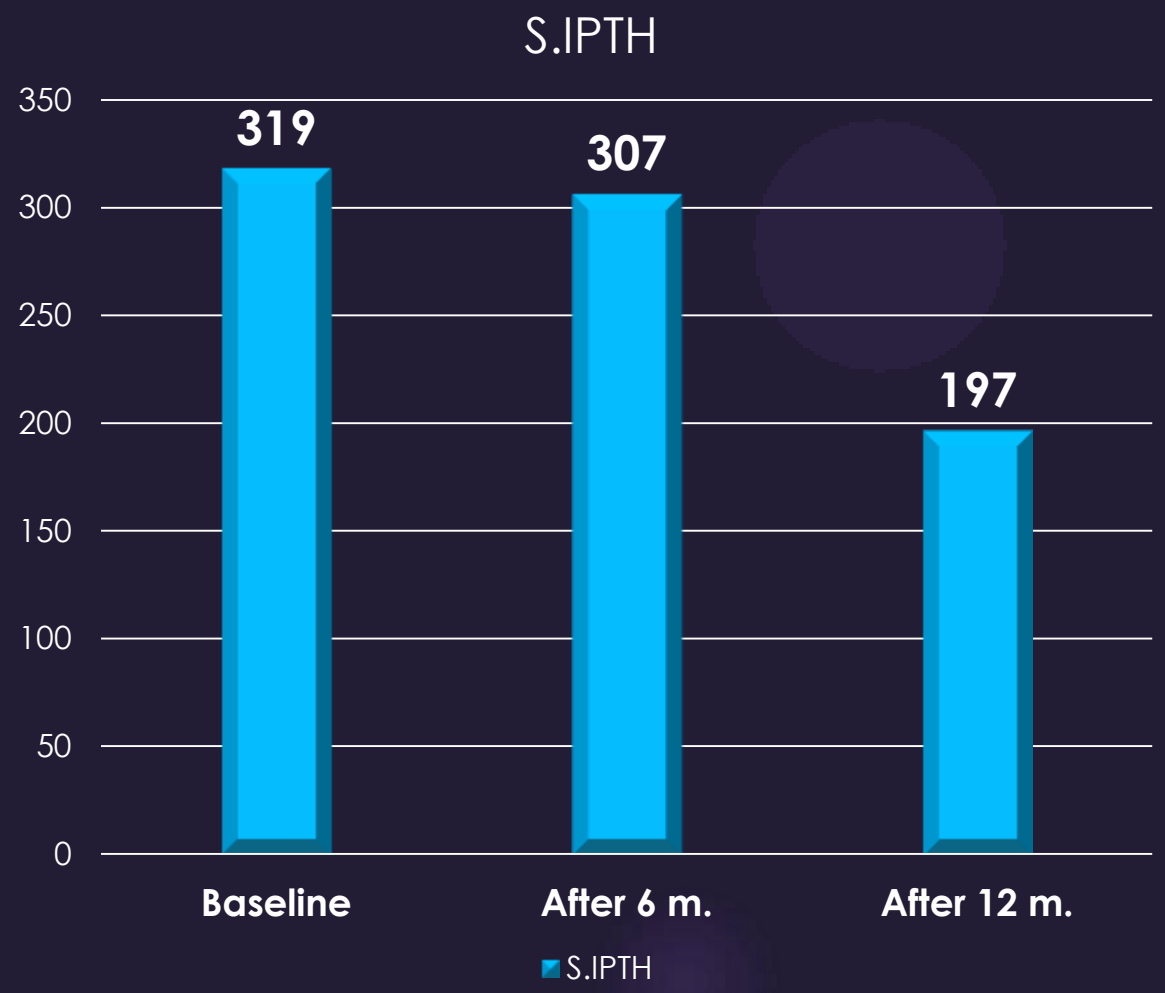
Ezio Movilli, Corrado Camerini, Paola Gaggia, Patrizia Poiatti, Alessandra Pola, Battista Fabio Viola, Roberto Zubani, Guido Jeannin and Giovanni Cancarini

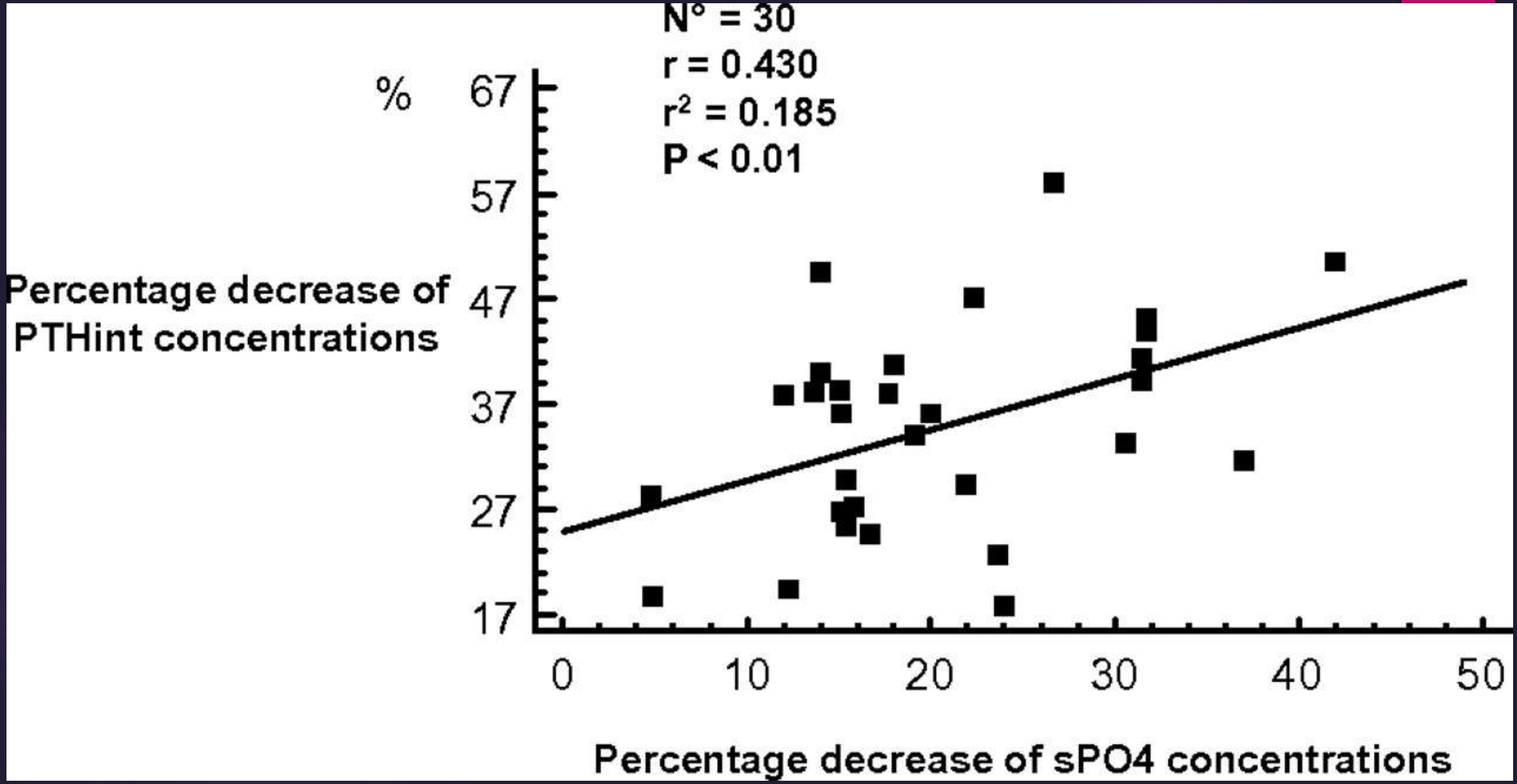
Division of Nephrology, Spedali Civili and Section of Nephrology University of Brescia, Brescia, Italy

Correspondence and offprint requests to: Ezio Movilli; E-mail: eziomov@libero.it

OL-HDF improve S.Ph and IPTH after shift from LF HD on 30 patients Nephrol. Dial. Transplant. (2011)







% change of pre-dialysis sPO4 concentrations and PTHint in Study group patients after the switch to OI-HDF

Phosphate control in dialysis

- major goal of chronic kidney disease–mineral and bone disorder (CKD–MBD) management, achievable through

- optimal dialysis removal,
- careful use of phosphate binders,
- and dietary phosphate control

THE PROBLEM

- dialytic removal does not equal the high P intake linked to the high dietary protein requirement of dialysis patients

HD strategy

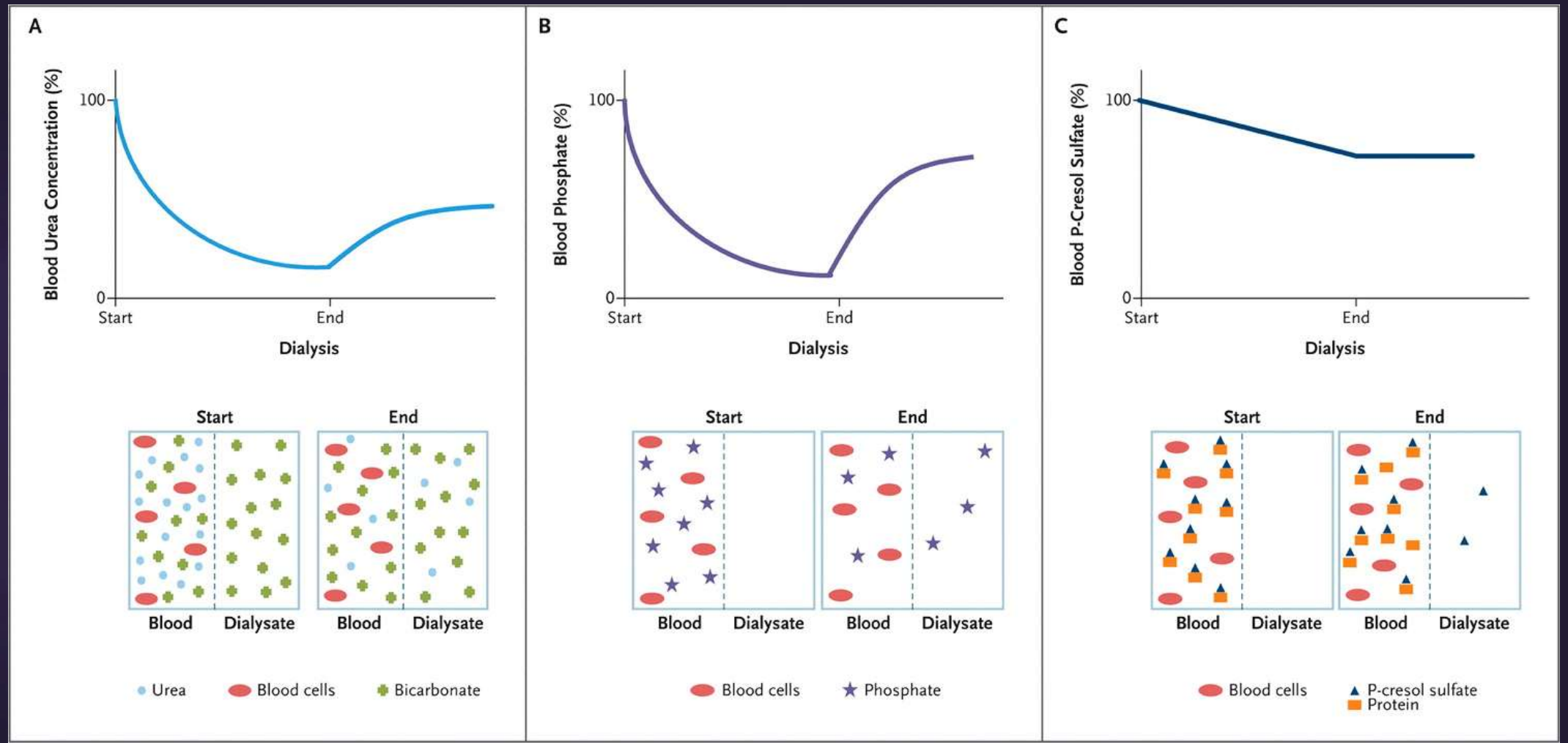
- Using a mixed diffusive–convective hemodialysis techniques, and increasing the **number and/or the duration** of dialysis techniques

The problem

- Phosphate kinetics during HD

Phosphate kinetics during HD

- The intradialytic output kinetics of P are completely different from that of urea or other small molecules for the different body volume distributions



Phosphate kinetics during HD

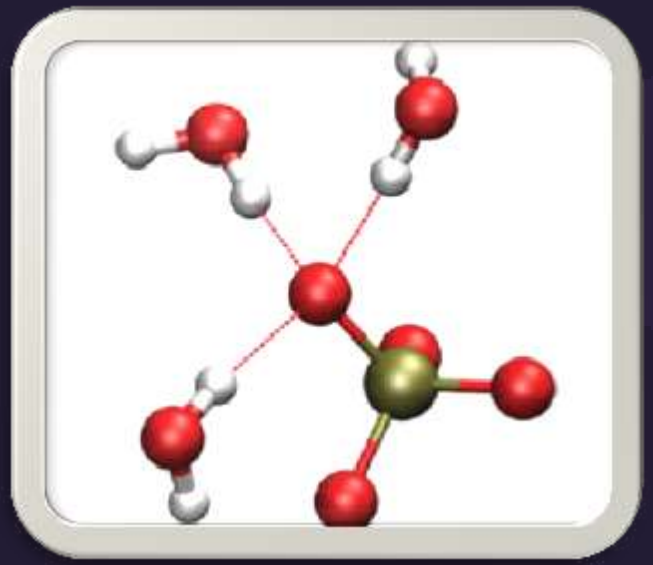
- mass transfer of P is hindered because this molecule, albeit of a low molecular weight, is

coated with water particles that bind strongly to P, thus transforming an originally small molecule into a molecule of medium dimension.

Phosphate kinetics during HD

J Comput Chem 29: 2330–2334, 2008

increased hydrated radius of “P “renders the passage through the pores of the dialysis membrane more difficult.



Typical hydration of a phosphate oxygen in solution.

Phosphate kinetics during HD

J Comput Chem 29: 2330–2334, 2008

- the P-oxyanion features a **higher charge (3−)**,
- further slowing the passage through the dialysis membrane. It is noteworthy that the three forms of P ions are approximately **spherical**, with an average van der Waals radius of more than 180 Å.

Phosphate Kinetics during HD

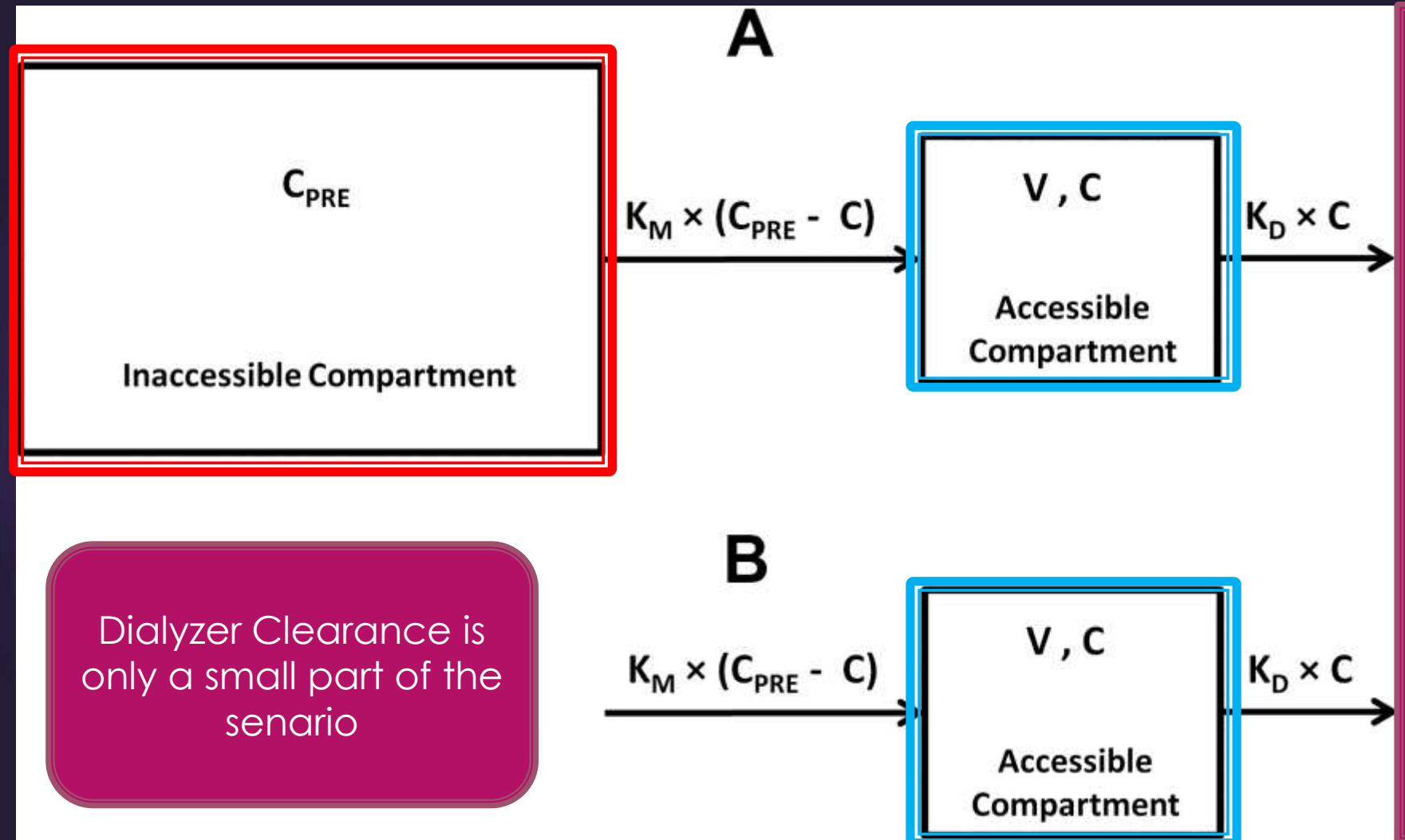
- **The 2 compartment model**

1- inaccessible compartment

2- accessible compartment

Phosphate Kinetics during HD

2016 by the American Society of Nephrology



Dialyzer Clearance is only a small part of the senario

C_{PRE}, predialytic plasma phosphorus concentration

C, instantaneous plasma phosphorus concentration;

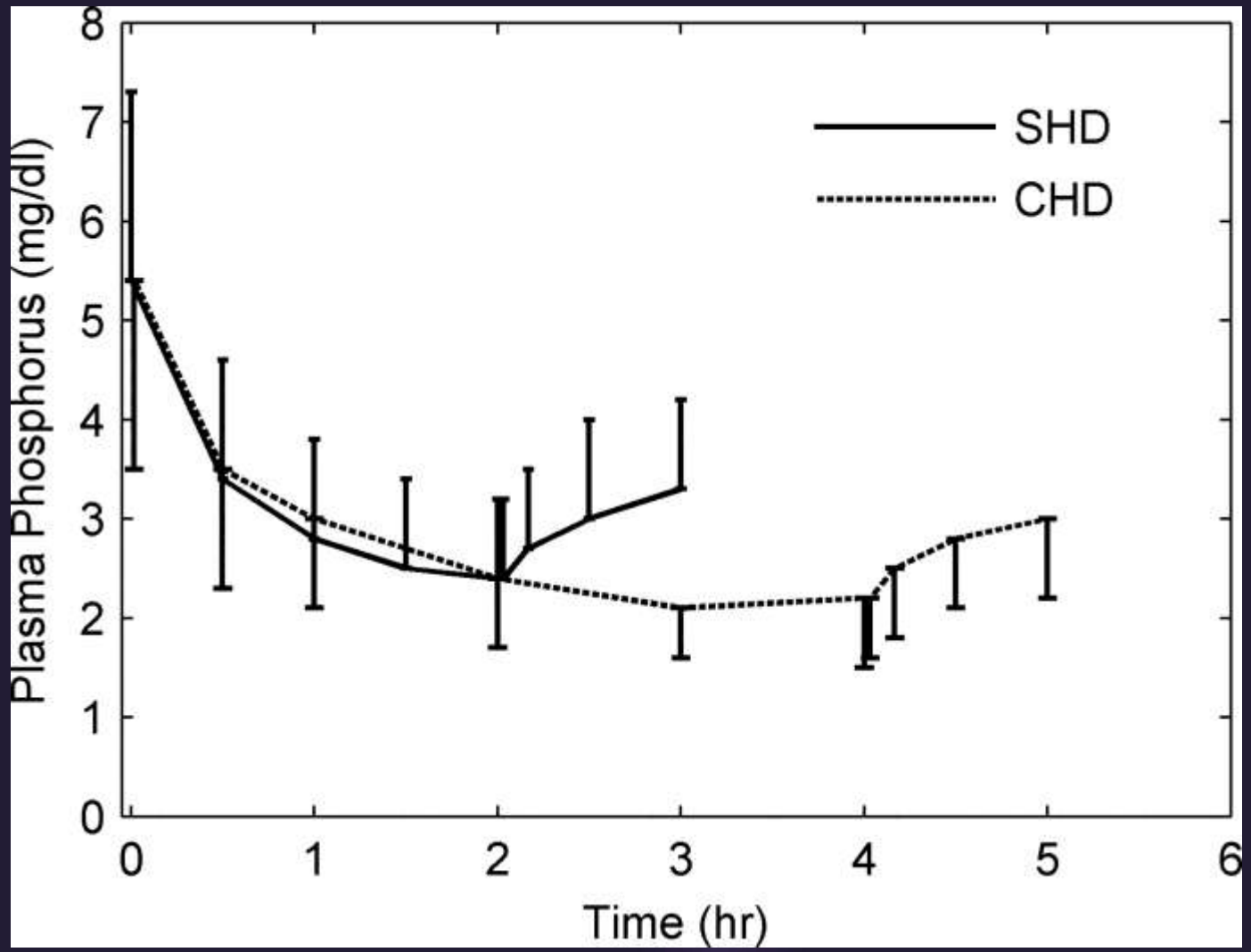
V, volume of accessible compartment for phosphorus;

K_M, phosphorus mobilization clearance;

K_D, dialyzer phosphate clearance

Phosphate Kinetics during HD

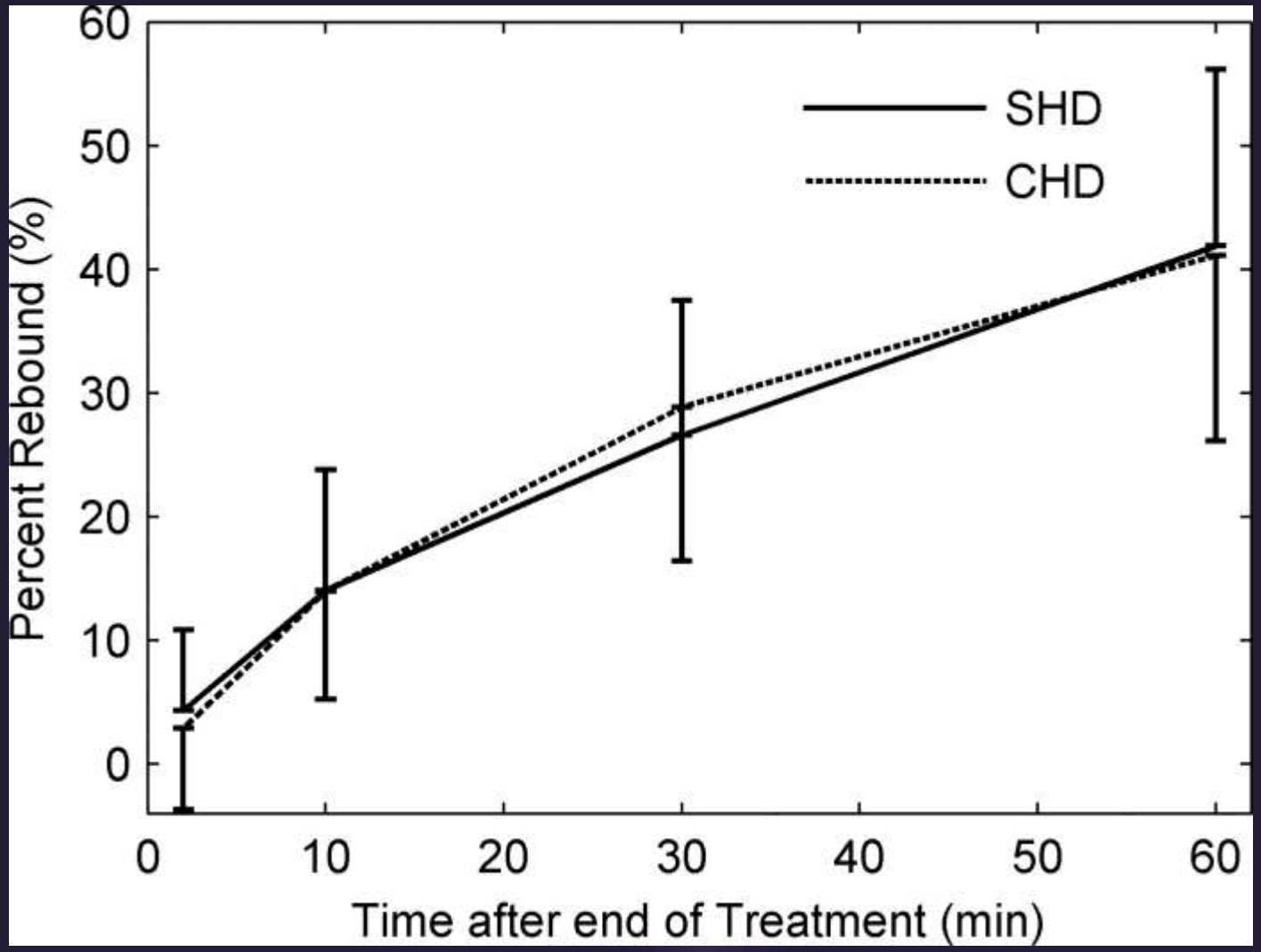
Plasma phosphorus concentration during and 1 hour after short hemodialysis (SHD) (solid line) and conventional hemodialysis (CHD) (dotted line) treatments



cjasn.org Vol 6 December, 2011

Phosphate Kinetics during HD

Percentage of rebound of plasma phosphorus concentration after short hemodialysis (SHD) (solid line) and conventional hemodialysis (CHD) (dotted line) treatments



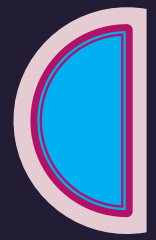
cjasn.org Vol 6 December, 2011

postdialysis P rebound

Blood Purif. 2006

multicompartmental distribution of P

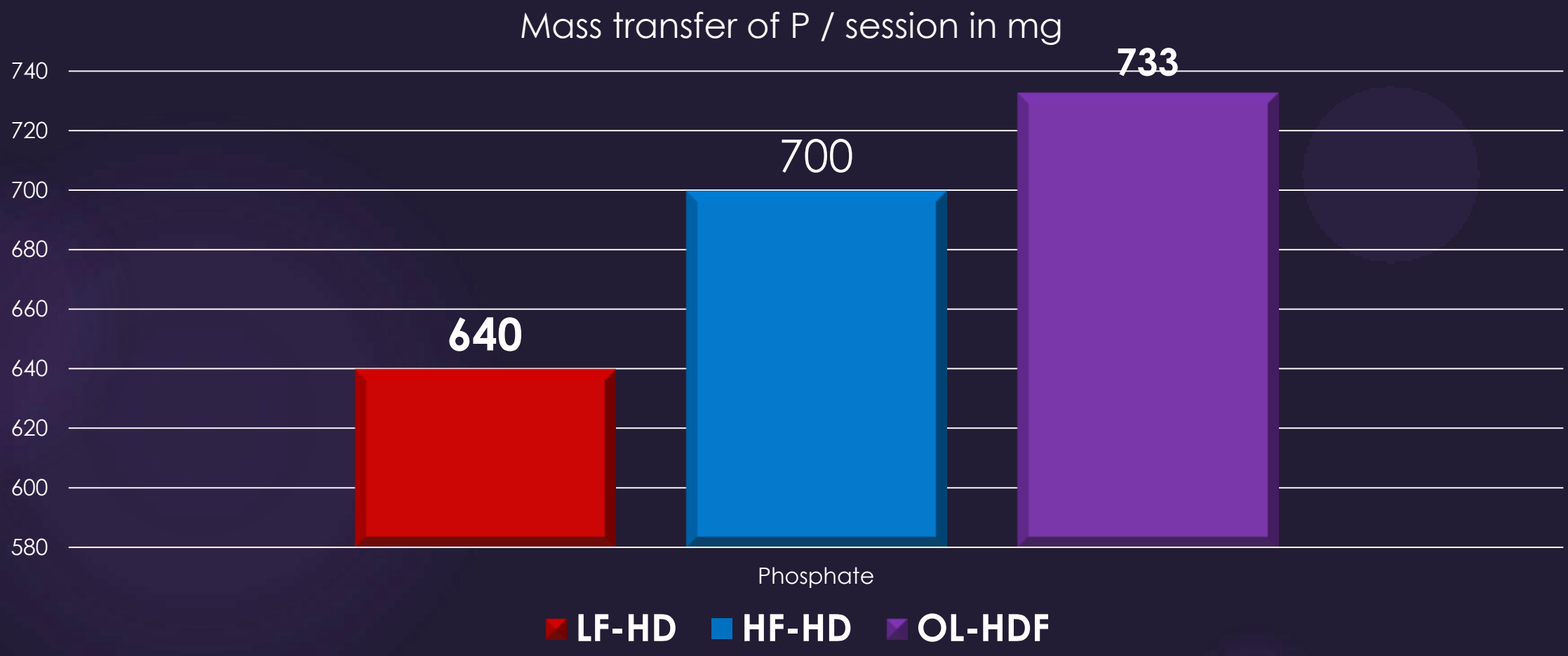
slow shift



Rebound

Longer HD sessions

Phosphate Kinetics Estimation during Hemodialysis



Nefrologia. 2007;27(1):

pre-midweek session calcium and phosphate levels in 5366 adult patients, 4515 treated by haemodialysis and 851 by on-line haemodiafiltration.

Nephrol Dial Transplant (2010) 25: 897–901
doi: 10.1093/ndt/gfp560
Advance Access publication 28 October 2009

The effect of dialysis modality on phosphate control: haemodialysis compared to haemodiafiltration–The Pan Thames Renal Audit

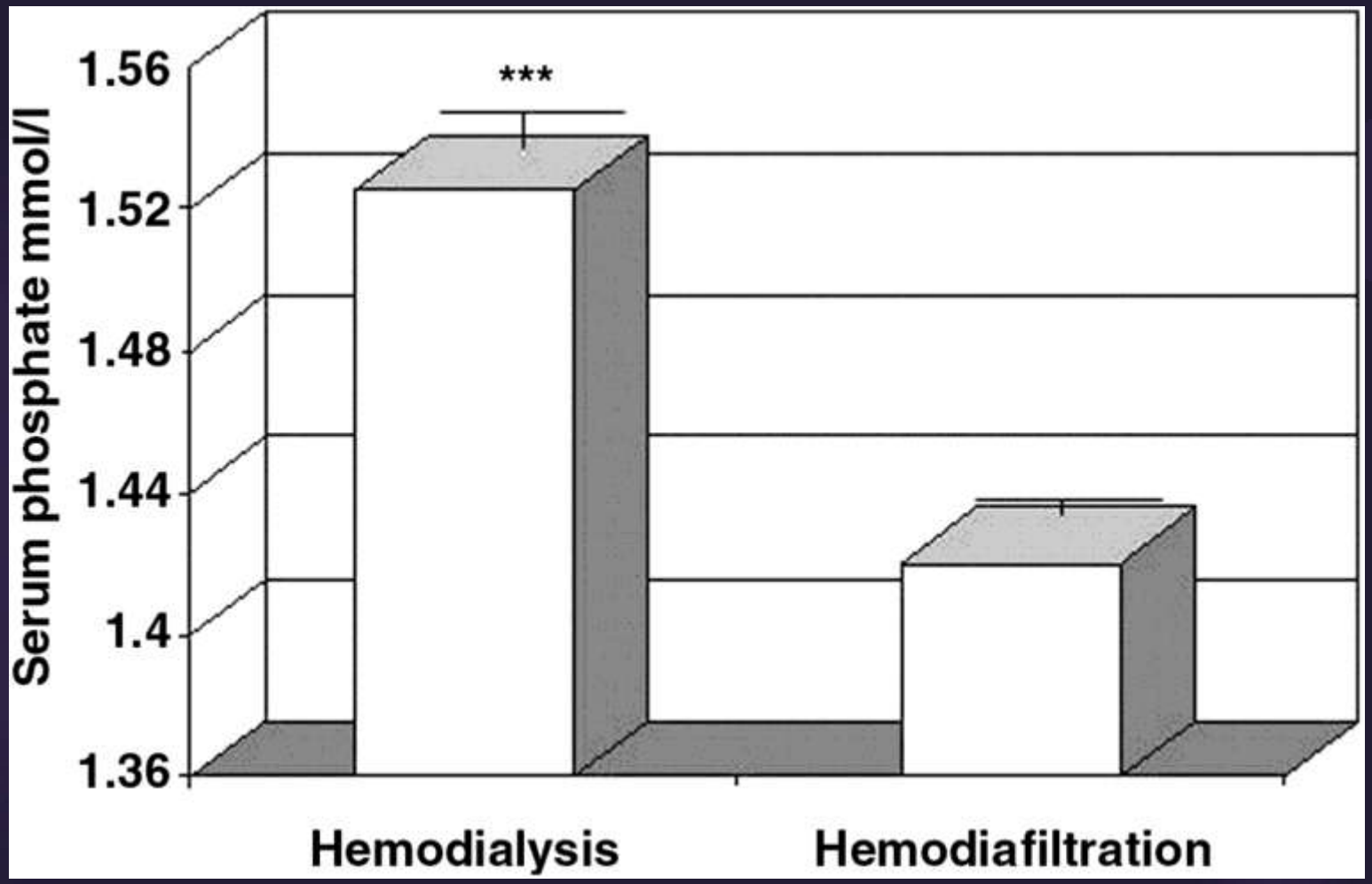
Andrew Davenport[1], Carrie Gardner[2], Michael Delaney[3]
and on behalf of the Pan Thames Renal Audit Group[4]

[1]UCL Centre for Nephrology, Royal Free Campus, University College London Medical School London, UK, [2]Audit, Information Analysis Unit, London Specialised Commissioning Group, London, [3]Kent Kidney Care Centre, East Kent University NHS Foundati• Trust, Canterbury, Kent, UK and [4]Pan Thames Renal Audit Group—see list

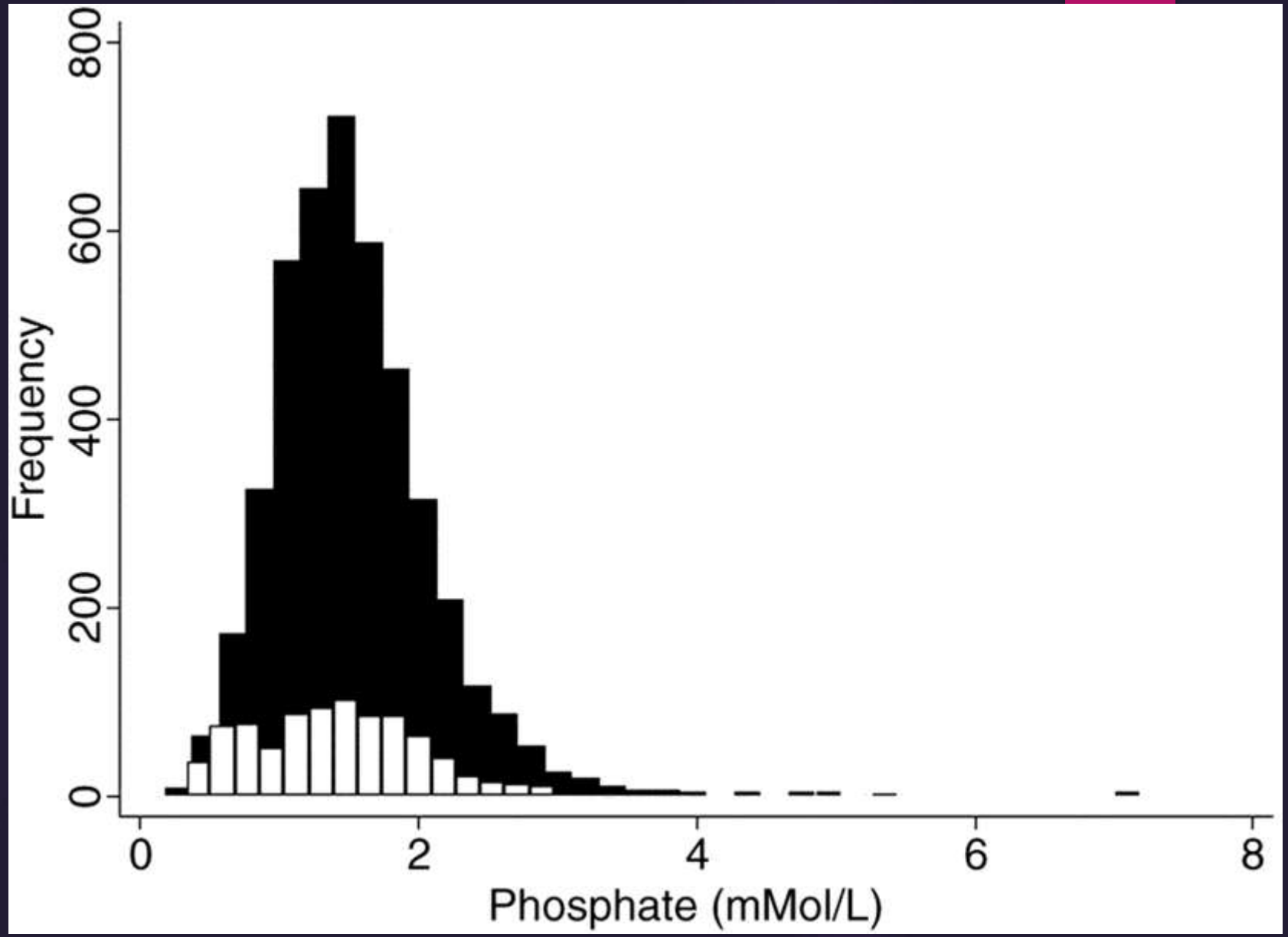
Correspondence and offprint requests to: Andrew Davenport; E-mail: andrew.davenport@royalfree.nhs.uk

Serum phosphate in hemodialysis and hemodiafiltration cohorts. Data expressed as mean (SEM). ***P < 0.001

Nephrol. Dial. Transplant. (2010) 25 (3):

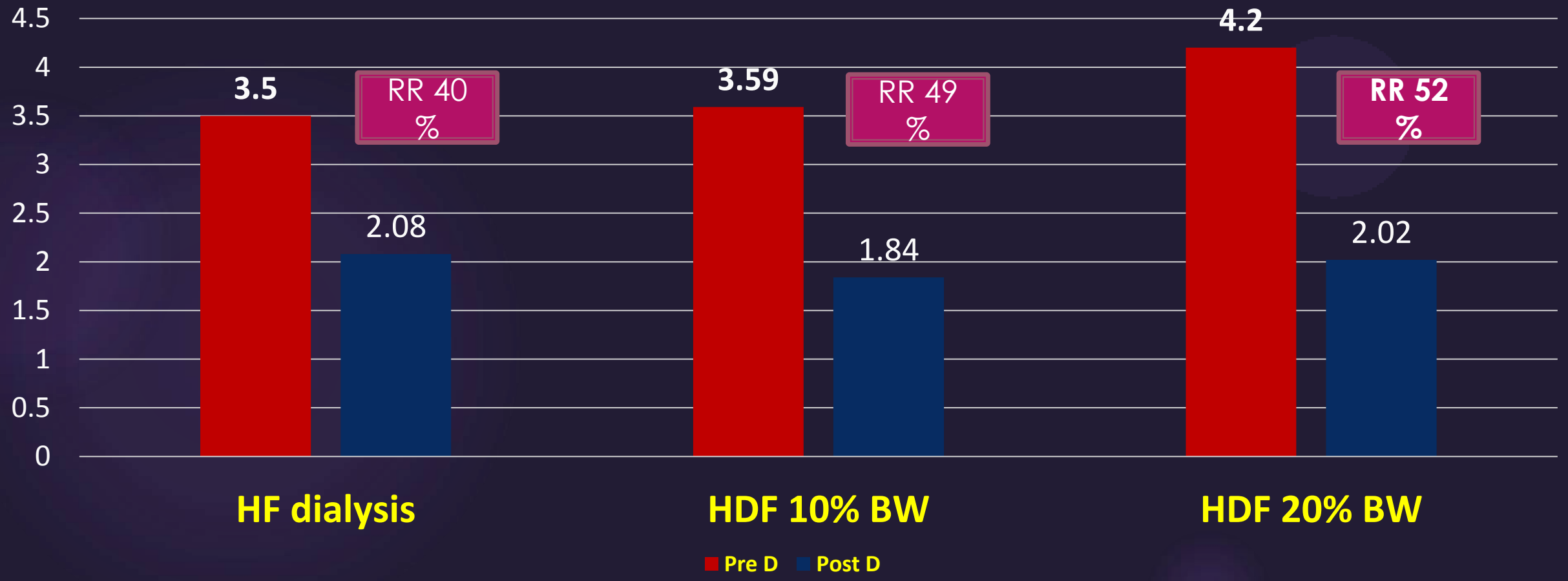


Frequency distribution curves of the pre-dialysis midweek serum phosphate concentrations in the haemodialysis patients (black bars) and haemodiafiltration patients (white bars).



Serum P with different HD modalities

13 patients study NEFROLOGÍA. Volumen 27.5. 2007



NDT Advance Access published September 29, 2013

Nephrol Dial Transplant (2013) 0: 1–16
doi: 10.1093/ndt/gft396

ndt
Nephrology Dialysis Transplantation

Original Article

Convective therapies *versus* low-flux hemodialysis for chronic kidney failure: a meta-analysis of randomized controlled trials

- Sixty-five (29 crossover and 36 parallel-arm) trials were identified (n = 12 182).

Table 2. Summary effect of convective therapies versus low-flux hemodialysis on the binary outcomes of interest

Outcome variable	No. of convective therapy study arms	No. of patients	Relative risk (95% confidence interval)	P value	Assessment of heterogeneity		Assessment of publication bias
					I^2 index, %[a]	Q-test P value	Egger test P value
All-cause mortality	21	4766	0.881 (0.759, 1.024)	0.09	18%	0.22	0.03
Cardiovascular mortality	3	3207	0.835 (0.711, 0.980)	0.03	0%	0.97	0.84
Infection-related mortality	2	2493	0.913 (0.716, 1.163)	0.46	0%	0.60	–
All-cause hospitalization	10	3952	0.912 (0.824, 1.011)	0.08	78%	<0.001	0.08
Therapy-related hypotension	12	1006	0.550 (0.347, 0.872)	0.01	99%	<0.001	0.85

[a]A measure of statistical heterogeneity across study results; an I^2 index $\geq$ 50% indicates medium-to-high heterogeneity.

Table 3. Summary effect of convective therapies versus low-flux hemodialysis on the removal of solutes in crossover and parallel-arm trials combined

Outcome variable	No. of convective therapy study arms	No. of patients	Absolute mean net change[a] (95% CI)	P value	Assessment of heterogeneity		Assessment of publication bias
					I^2 Index, %[b]	Q-test P value	Egger test P- value
Parathyroid hormone (9225 Da)							
Pre-therapy serum level, pg/mL	11	1192	−20,74 (−45,56, 4.08)	0.10	89	<0.001	0.30
Pre-therapy serum inflammation markers							
C-reactive protein, mg/L	17	1156	−0.14 (−0.57, 0.29)	0.52	37	0.06	0.01
Interleukin-6, pg/mL	7	284	−0.42 (−0.73, −0.11)	0.01	0	0.62	0.85
Superoxide dismutase, U/gram Hb	2	47	115.82 (9.01, 222.63)	0.03	0	0.67	–
Total antioxidant capacity, mmol/L	2	47	0.11 (−0.10, 0.32)	0.30	88	0.005	–

Long term outcome between HF-HD and HDF

CJASN December 2009 vol. 4 (858 patients)

Parameter	Group	3 Mo	6 Mo	12 Mo	24 Mo	36 Mo	48 Mo	60 Mo
Phosphate (mmol/L)	HD mean	1.68	1.79	1.72	1.78	1.81	1.71	1.64
	HDF mean	1.75	1.80	1.82	1.92	1.75	1.86	1.79
	P	**0.273**	**0.873**	**0.060**	**0.019**	**0.370**	**0.039**	**0.121**
PTH (pmol/L)	HD median	30.3 (36.0)	28.0 (36.1)	25.4 (38.0)	27.2 (38.8)	26.0 (44.0)	30.0 (42.7)	37.0 (57.0)
	HDF median	23.0 (38.0)	26.0 (34.7)	25.1 (38.6)	32.3 (39.0)	35.2 (49.4)	37.5 (47.4)	45.0 (52.3)
	P	**0.489**	**0.450**	**0.488**	**0.045**	**0.141**	**0.289**	**0.197**

A cross-over design of 3 periods (6m each on 51 patients) BMC Nephrology , 2015

	HDF1	HD	HDF2
Phosphataemia (mmol/l)	1.58 ± 0.2	1.59 ± 0.3	1.61 ± 0.2
iPTH (pg/ml)	215 ± 110	220 ± 111	245 ± 108
Cinacalcet mg/d (%)	52 (5.8)	52 (5.8)	47 (7.8)
Sevelamer unit/d (%)	3.3 ± 4 (31)	3.4 ± 4 (33)	4 ± 4 (33)

ORIGINAL ARTICLE

JNEPHROL 2013; 26(02): 342-349

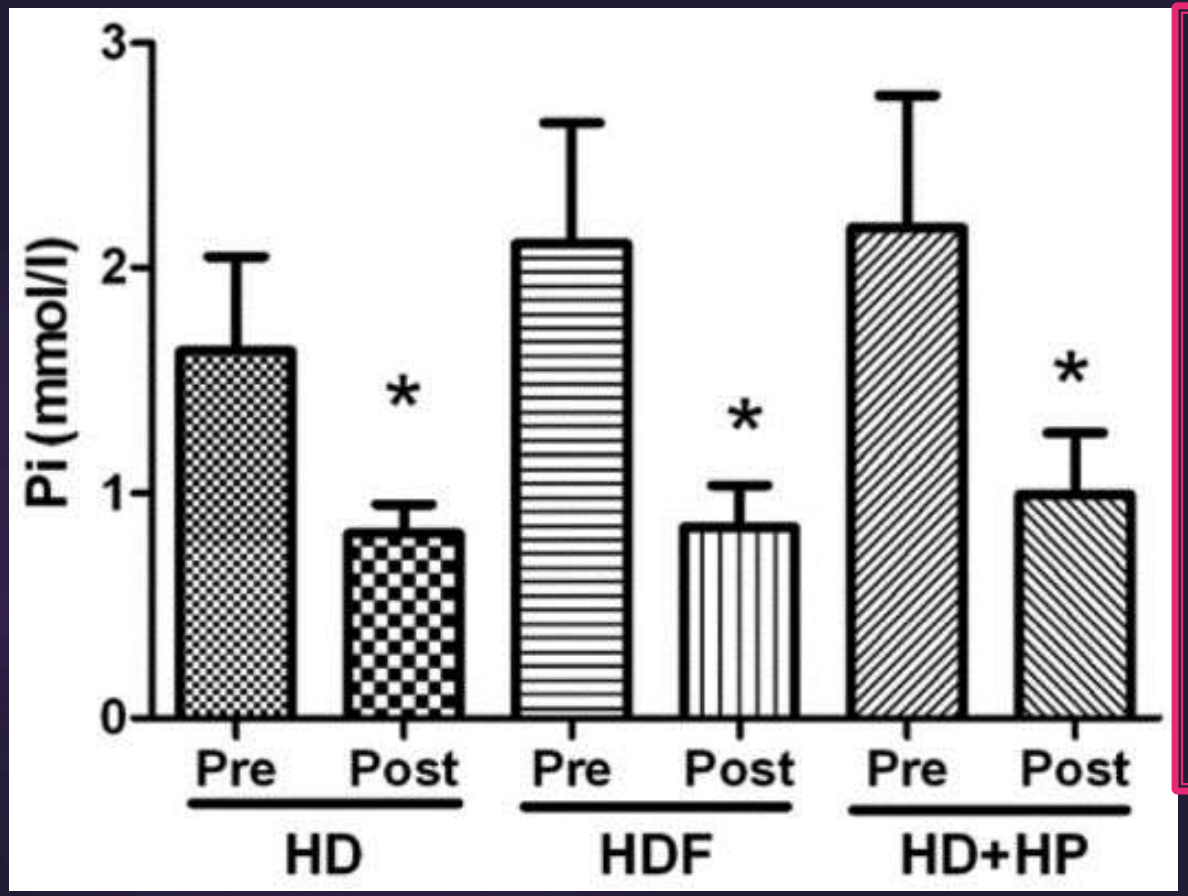
DOI: 10.5301/jn.5000150

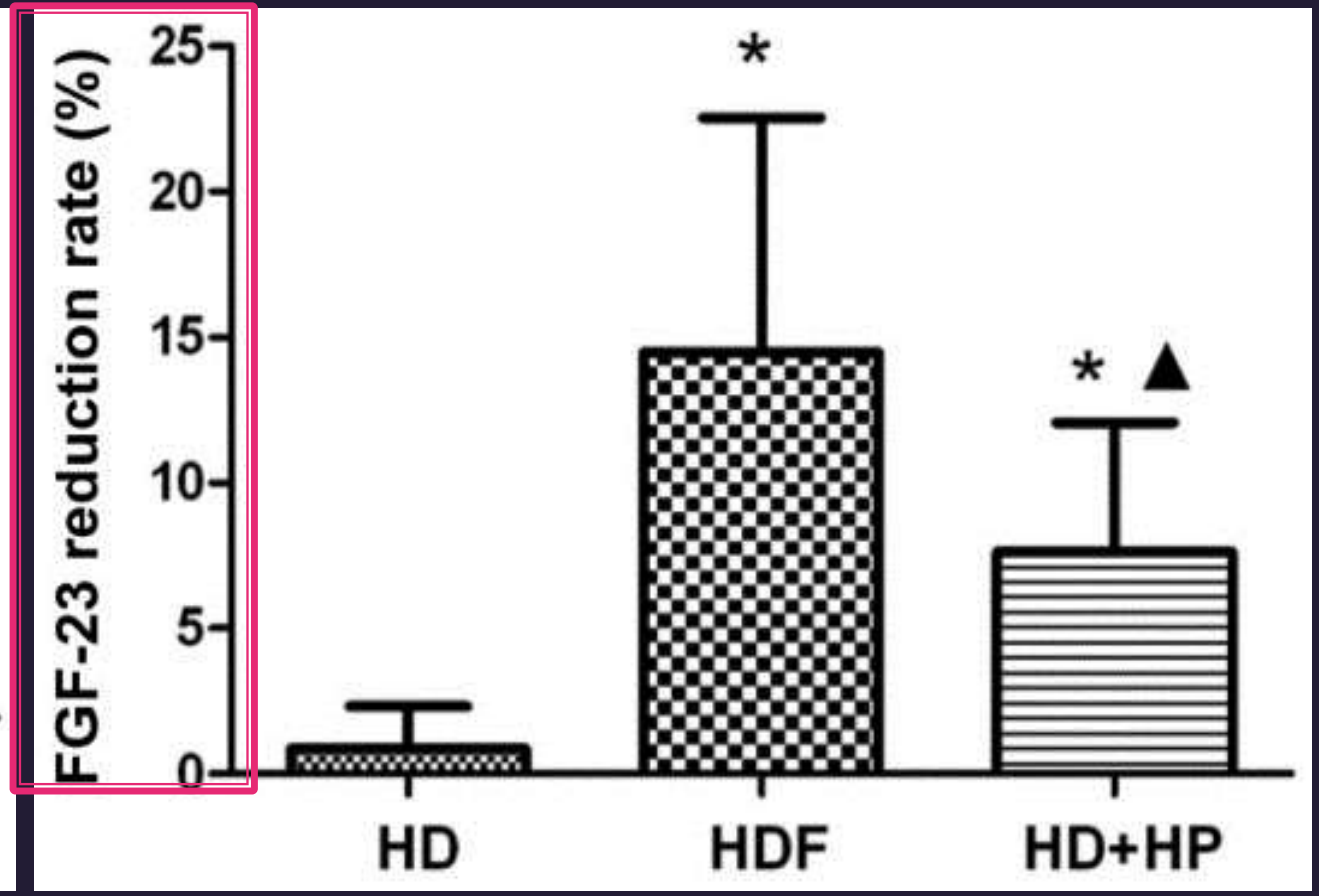
FGF-23 removal is improved by on-line high-efficiency hemodiafiltration compared to conventional high flux hemodialysis

Fifty-three patients were included in the HD group

while 32 patients were included in the OL-HDF group

What is effect of Dialysis on FGF23 level ?

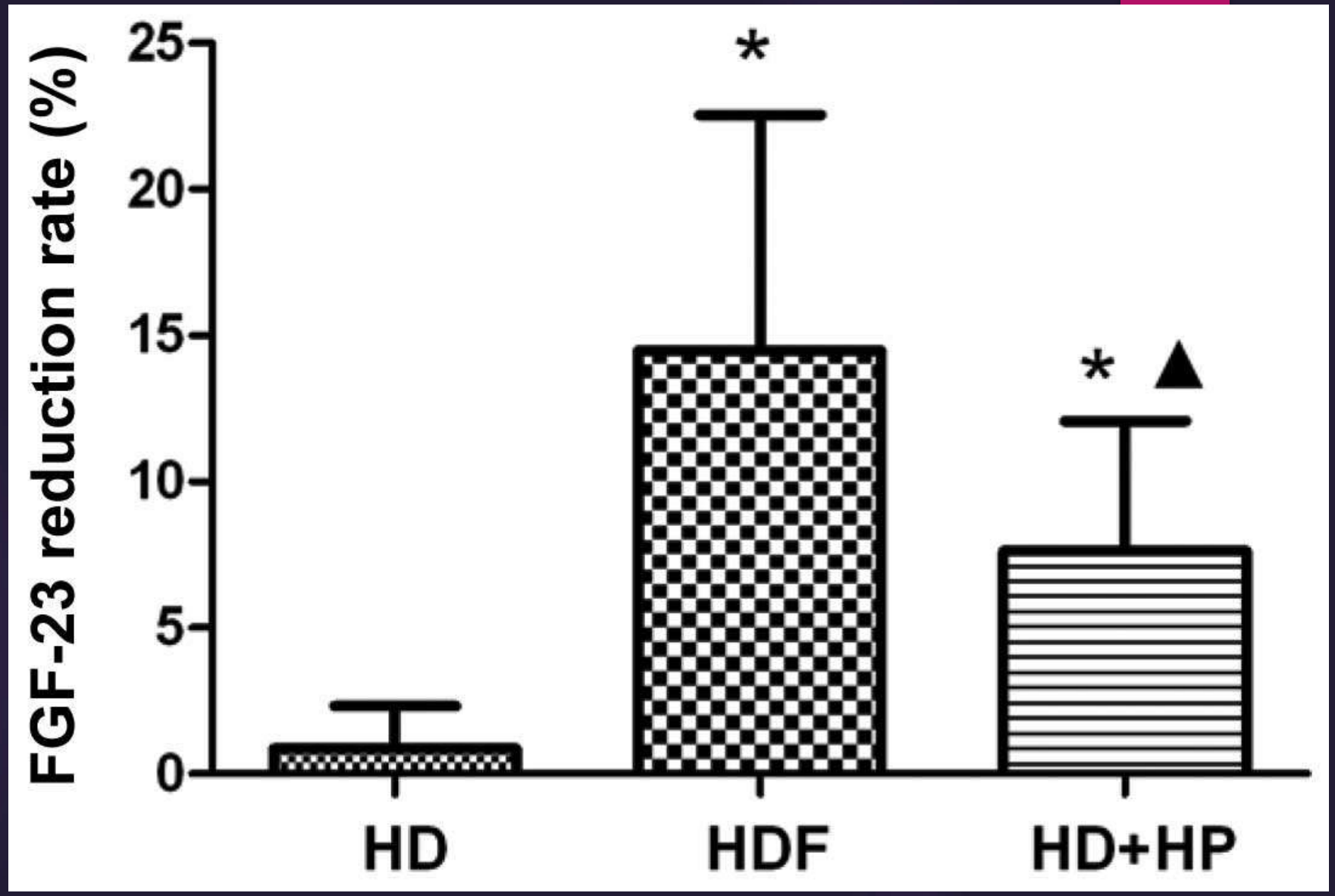




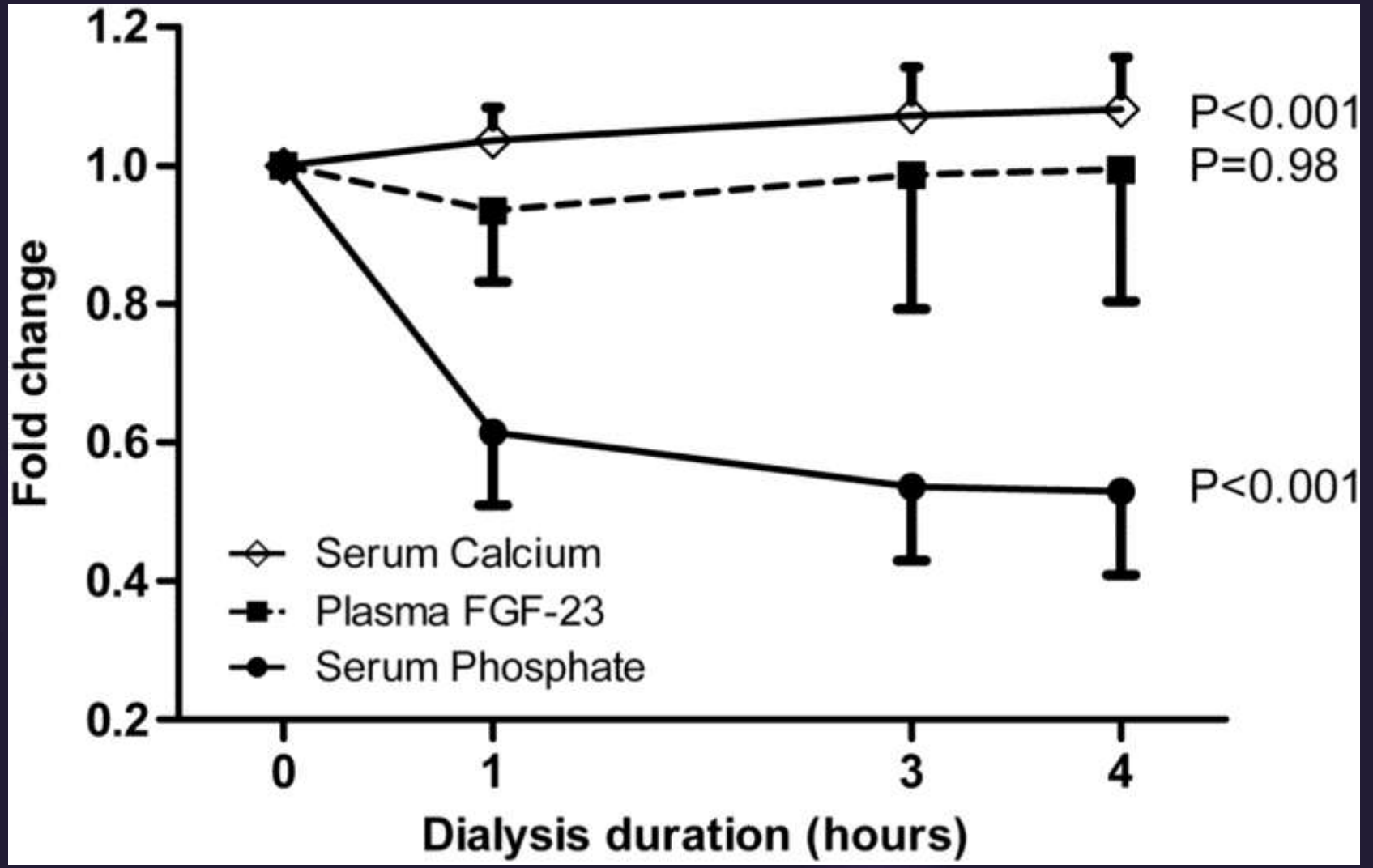
Exp Ther Med. 2014 Apr; 7(4): 947–952.

FGF23 RR %

April 2014
Volume 7 Issue 4



FGF23 during Low Flux HD



Nephrol. Dial. Transplant

: November 24, 2015

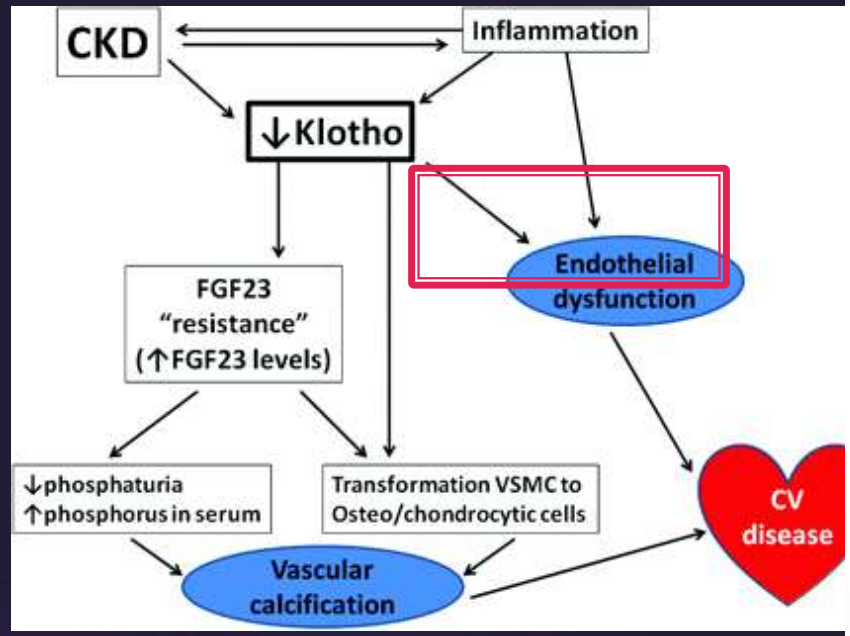
JNEPHROL 2013; 26(02): 342-349

	Concentration		Reduction rate	Clearance	Kt/V
beta2-microglobulin	**Pre (mg/L)**	**Post (mg/L)**	**%**	**mL/min**	
HD	23 [17.2-39.8]	6.2 [2.8-12.1]	72.8±6.2	92.6±23.1	1.7±0.3
OL-HDF	27.8 [9-44.5]	5.3 [1.7-7.9]	80.8±4.0	108.5±25.7	2.0±0.3
P	*NS*	*NS*	*<.0001*	*.0104*	*<.0001*
FGF-23	**Pre (RU/mL)**	**Post (RU/mL)**	**%**	**mL/min**	
HD	1630.2 [194.4-14694.4]	984.3 [108.2-5626.2]	36.2±28.6	41.8±20.7	0.7±0.4
OL-HDF	1685.9 [231.1-23907]	691.1 [97.4-10529.7]	55.7±25.2	55.0±29.7	1.0±0.4
P	*NS*	*NS*	*.0001*	*.0150*	*.0001*

Conclusion

- Does HDF will help in CKD-MBD ?

  Players , Mediators , or Endothelium



Vascular calcification
Too many pieces to be add

Thank you